R. J. Cole.

11 June. 1928.

HOW WE INHERIT

BY

EDGAR ALTENBURG

ASSISTANT PROFESSOR OF BIOLOGY
THE RICE INSTITUTE, HOUSTON, TEXAS

NEW YORK
HENRY HOLT AND COMPANY

PRINTED IN THE
UNITED STATES OF AMERICA

PREFACE

Heredity is, for the average person, one of the most interesting fields of biology, especially when it concerns itself with human beings. Strip it of the element of human interest, and it becomes, for many people, a dry subject. But the principles of heredity were, for the most part, discovered in connection with the lower forms of life, and it might seem, offhand, that no serious treatment of the subject could do otherwise than to limit itself largely to non-human material. Yet this is not necessarily true. Just because a falling apple is supposed to have attracted Newton's attention to the laws of gravitation, does not mean that for all time apples must be used in trying to impart a knowledge of these laws to others. Any convenient material will do for the purpose. So in heredity. If human beings can be used in the development of a principle, or in arousing interest in the principle, then so much the better. We now know enough about heredity to believe that we ourselves conform to the same general principles as do the lower forms of life, as shown by those cases of human heredity that have been sufficiently well worked out to be trustworthy. These should be used when possible in the general treatment of the subject. But the matter must not stop here. The student must, by all means, know the actual materials that have been used by the geneticist in the study of heredity. Once his interest has been stirred up through the channel of human appeal, then it is time enough to go to the lower forms of life and to show him how they served in establishing the principles. This I have attempted to do in the present treatment. The subject matter has been chosen so as to illustrate each of the major phases of the subject, and particularly the

more modern developments concerned with hereditary processes that are important in nature, or to man.

It was thought best not to litter up the book with numerous cases of heredity which were essentially repetitions of the same general principles. At the same time, it is desirable that the student should have a working knowledge of the subject. To meet this need, I have prepared a series of "reports," which are being separately published, and which, among other things, leave many of the special cases to the student himself.

The book presupposes no previous knowledge of biology, so that the general reader should be able to get an understanding of the subject through its perusal.

E. A.

March, 1928.
The Rice Institute,
Houston, Texas.

CONTENTS

HOW WE INHERIT

CHAPTER I

REPRODUCTION

With the aid of the microscope there is revealed to us a picture of living substance which we little suspect it of having from mere examination with the naked eye. Take any part of the body — a small fragment of skin from the back of the throat — and look at it under a magnification of about 500 times its actual

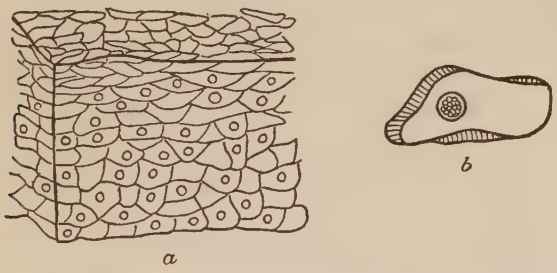

FIG. 1. The skin of the throat as seen under the microscope: *a*, a small fragment; *b*, a single cell from the fragment, more highly magnified.

size. You notice at once a surprising thing: the entire lining of the throat is chopped up into minute units (see Fig. 1*a*). These the biologist refers to as cells.

Now focus your attention upon a cell — any one will do — and magnify it still further. Look carefully at its contents and there, in the middle of the cell, you see a spherical body — the nucleus (see Fig. 1*b*).

Turn your attention to almost any part of the body, and you notice that it has essentially the same structure as the lining of the throat — it consists entirely,

or in large measure, of nucleus-containing units — cells. Convince yourself of this by going to some other part of the body — the muscular wall of the stomach. Examine a small fragment of it under the microscope, and again you notice that it is chopped up into units, this time shaped somewhat like toothpicks (see Fig. 2*a*). Inside each one of them you see a nucleus and you have no difficulty in recognizing them as cells.

Continue to explore the body with your microscope. Examine the lining of the intestine and you see cells that look like a lot of little bricks side by side (see Fig. 2*b*). Pass on to the brain. This time you see cells that are drawn out into long fibres (see Fig. 2*c*). Get next a small drop of blood from your finger and see the red blood cells — millions in every drop — each shaped somewhat like a silver dollar, round and flat (see Fig. 2*d*). You would look in vain for a nucleus in any of the red blood cells, but each of them possessed a nucleus at one time and has lost it.

Go now to a bone and shave off a small speck of the gristle that forms a cap at the end of the bone. Here you have an apparently lifeless material. But look at it under the microscope and you see cells scattered about (see Fig. 2*e*) in its substance. Lifeless material separates the cells from each other, but even this the cells have formed.

Everywhere in the body you see cells, not always of the same shape to be sure, but all of them agreeing in at least one respect — the possession of a nucleus at some time during their existence. So universal are cells in the structure of all living substance, that you could, in most cases, tell whether or not a small frag-

ment of substance was derived from a living thing by looking for its cellular structure. Even the lifeless portions of plants and animals consist either of dead cells, as our hair, or of the products of cellular activity, as the material of which gristle and bone largely consist.

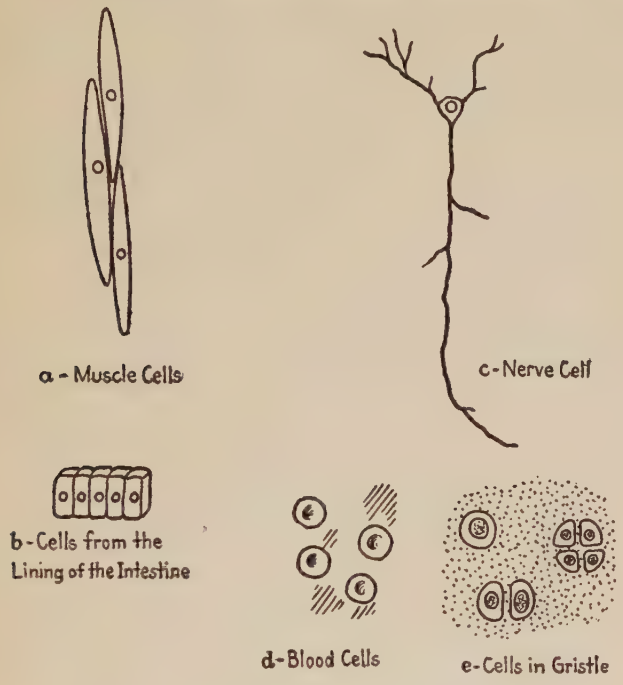

Fig. 2. Cells from various parts of the body.

The living substance itself fills the cell. This substance is so important that it deserves a special name. Biologists call it protoplasm. It is convenient to refer to the protoplasm outside of the nucleus as the cytoplasm, but both the nuclear material and the cytoplasm are living substance — protoplasm. Under the microscope, protoplasm has a transparent appearance.

The nucleus is denser than the surrounding substance in the cell and stands out somewhat like a piece of ice in water.

You would naturally expect the operation of living substance to be explained, in part at least, by its structure, just as you would the working of a watch or any other mechanism. The cell should have something to do with the operation of living substance and help to explain some of the secrets of life. The discovery of cells has in fact been of great value in explaining many life-operations. In connection with the nucleus especially, there are structures which have been found to be at the basis of one of the most important of life-operations; namely, the transmission of the units of heredity from parents to offspring. And it is about the cell that the processes of reproduction and development centre.

The origin of a new being seems an almost mysterious thing. How do we begin our existence, what are we like when we start life, and how do we develop from apparently almost nothing? When you were born, you had already passed through the principal stages of your development and you were practically a completely formed human being.

Suppose that a moving picture had been taken of your development before birth and that you now reversed the film and traced your development backwards to its very beginning. You would see yourself becoming not only smaller and smaller, but also simpler and lacking at certain early stages limbs, head, etc.; and you would gradually approach a spherical shape. (See Fig. 3.) At the beginning of your development, you see

yourself just as a microscopic speck of living substance, perfectly spherical in shape. It is difficult to imagine just how small you were at the beginning of your existence. You and I and the rest of the human race, a billion and a half of us in all, could at this very earliest stage in our development have been crowded into a two-gallon bottle.[1]

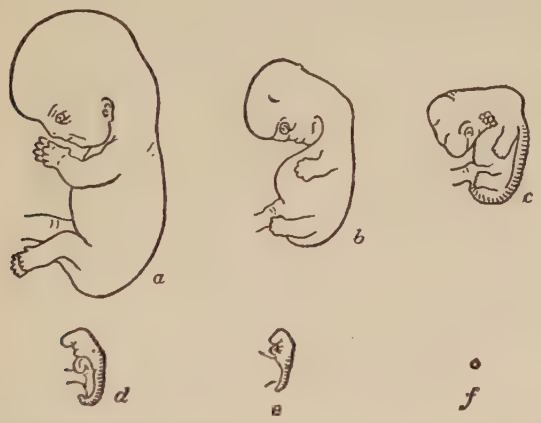

FIG. 3. Development (reversed). The embryo is shown at earlier and earlier stages.

But so far you have looked merely at certain external changes that were going on. Suppose your body had been semi-transparent and that the moving picture had recorded the internal changes. Again trace your development backwards. You now see your internal organs gradually becoming simpler, your muscles, nerves and other tissues gradually losing their distinctive character and all parts assuming a more or less uniform appearance. At this stage you were so small

[1] According to an unpublished estimate made by H. J. Muller, of the University of Texas.

that a microscope must have been used in making the pictures. (See Fig. 4.)

Now focus your attention on the cells of your minute body and you see immediately why you have no definite tissues; for all your cells are alike, more or less spherical in shape. They remind you somewhat of oranges tightly packed together in a box. At this stage in development, your cells are said to be "undifferentiated." They have not yet the definite shapes that they

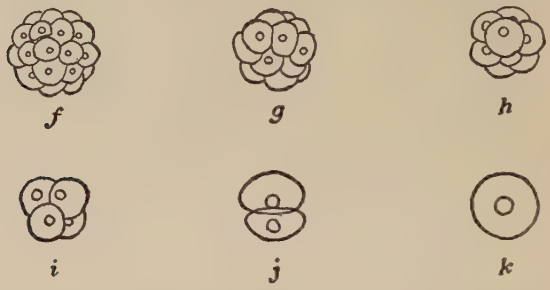

FIG. 4. Development of a lower animal, the rabbit, traced backwards through very early stages, even earlier than *f* of Fig. 3, highly magnified.

later assume when they "differentiate" to form muscle, nerve, skin, etc.

Another thing that you would notice as you traced your development backwards is that the number of cells becomes fewer and fewer in accordance with the diminishing size of the body. (See Fig. 4.) At the very earliest stage in your development you would see just one cell. This is the microscopic sphere of living substance previously referred to when it was stated that the entire human race, at this stage in its development, could be gathered together into a two-gallon bottle. The single cell with which you began your existence is

known as the fertilized egg (or fertilized ovum). You could at once identify it as a cell by the presence within it of a nucleus.

Turn our film forward and you will see the fertilized egg do a peculiar thing. It chops itself into two through

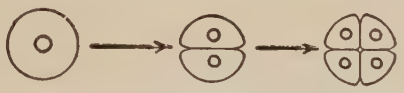

FIG. 5. Division of the fertilized egg as seen in some lower animals, such as the starfish, which sheds its eggs in the water. The human egg has not been seen at these very early stages.

the middle and so makes two cells out of itself. (See Fig. 5, also Fig. 6). This process is known as cell division. Each of the two new cells repeats the process and to-

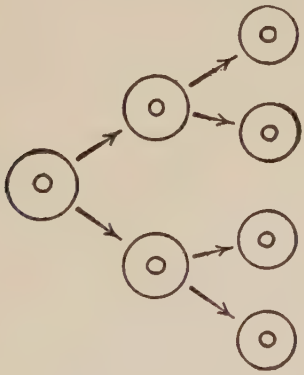

FIG. 6. Schematic representation of cell division. The cells are shown separated from each other after their division. They actually remain together.

gether they form four cells. From these are formed eight cells; then 16; 32; 64, etc., until the billions of cells are produced that constitute the fully developed body. Focus your attention on an undifferentiated cell and you

see it grow to a certain size and then divide into two. The new cells are each half the size of the parent cell, but they grow and repeat the process of cell division. This continues until differentiation sets in. After a cell is differentiated it is as a rule no longer capable of division.

When you hear someone refer to an egg, you are apt to think of an object that we associate with a hen. One hardly suspects that a thing of such great size as a hen's egg is a cell or that it has anything in common with the human egg. As a matter of fact, the part of the hen's egg that you ordinarily refer to as "yolk" is a cell, but one that is gorged with yolk, the lifeless food material that nourishes the developing chick. The hen's egg, however, has a living part, and this does not differ greatly in amount from that of the human egg or any other species. The living part is just a microscopic speck of transparent substance resting on the top of the yolk. So minute is the speck of living substance in the hen's egg, that it ordinarily escapes observation; but it is, none the less, the essential part of the cell. Within this clear speck you can see the nucleus with the aid of a microscope. You could by stuffing the human egg full of a lot of yolk, bloat it up and convert it into something that looks like a hen's egg; in the process the protoplasm would be shoved to one side and flattened out into the disk-like speck referred to in connection with the hen's egg. The human embryo is nourished within the mother during its growth, and requires no yolk for its development. The egg-size of different animals varies greatly, from the microscopic dimensions of a human egg to the

enormous size of an ostrich egg, differences which are due almost entirely to the varying amount of yolk in the egg.

Now an ordinary egg cell is incapable of development; it must first undergo a change, known as fertilization, in which an element from the male is concerned. In the reproductive material derived from the male, the spermatic fluid, there are many millions of microscopic particles (see Fig. 7*a* and *b*) each shaped somewhat like a tadpole with a so-called "head" and a "tail," but each almost inconceivably small; in fact, much smaller

FIG. 7. The spermatic fluid of a frog, *a*, as seen under low power, showing numerous minute bodies, the sperm cells; *b*, one of the sperm cells highly magnified.

even than a microscopic egg cell. By means of snake-like movements of their tails the exceedingly minute bodies from the male are capable of swimming to an egg and boring their way into it. After just one of the wriggling male particles has entered it, an egg is capable of development, and is said to be fertilized.

Insignificant as may seem the microscopic bodies derived from the male — because of their almost infinitesimally small size — they are nevertheless of immense importance; and in fact, each one is a cell, modified in shape in a manner such that swimming movements are easily possible. The cells in question which the male produces are known as the sperm cells. Fertilization,

then, involves the union of two cells: an egg cell derived from the mother, and a sperm cell from the father.

Sperm and egg cells are produced in the reproductive organs — the testes in the male and the ovaries in the female. (See Fig. 8.) In some animals, as the frog, fertilization occurs in the water. In this species the female sheds her eggs into the water and the male, who

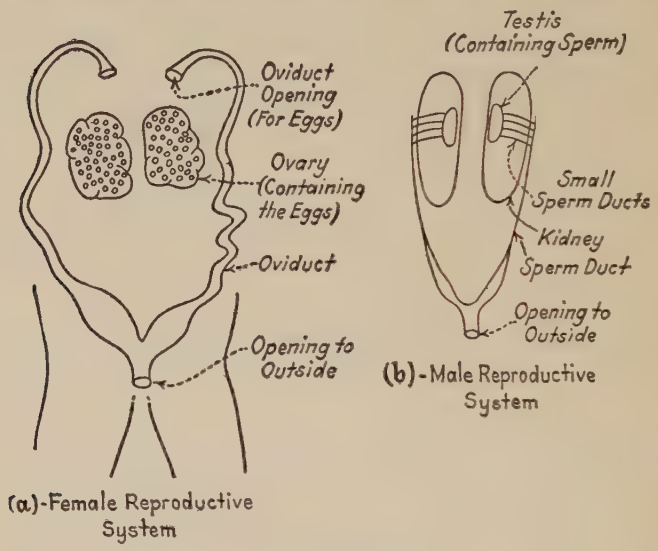

Fig. 8. The reproductive organs of the frog.

is clinging to her in the act of copulation, sheds his sperm also into the water. The reproductive cells reach the outside by means of tubes or ducts, the oviducts in the female, the sperm ducts in the male. It is a curious fact that the oviducts do not connect at their inner ends with the ovaries, so that the ripe eggs have to burst through the thin membrane that lines the ovary, pass through an open space and into the open end, or funnel,

of the oviduct. This arrangement applies to practically all the backboned animals, including man. In the hen, the oviduct is somewhat unusual as regards its great length, a peculiarity connected with the fact that as the eggs pass down the oviduct they become surrounded by the white of the egg, which is oozed out of the wall of the oviduct along the greater part of its length.

In most of the higher animals, fertilization occurs in the body of the female. The sperm is received during copulation in the lower end of the oviduct and fertilization occurs here or further up. The sperm cells are continually being produced in the testes during the adult life of the male and they are passed to the enlarged lower end of the sperm duct, where they are stored. They are mixed with a fluid produced by glands connected with the lower end of the duct and they are now ready to be passed out or ejaculated, at the time of copulation.

In all animals, the number of sperm cells shed at an ejaculation is far in excess of the eggs. In the case of man, the figure exceeds 200 million sperm cells, any one of which suffices for fertilization; and indeed, should more than one enter the egg, development would be abnormal or impossible. There is, however, some sort of reaction on the part of the egg which prevents any more sperm cells from entering after contact with the first one.

If you should look at a human sperm cell under a very powerful microscope, you would see distinctly the "head" and the long slender "tail" (see Fig. 9). The "head" is shaped somewhat like your open hand, broad in one view, narrow in the other; and when seen in

either view, it tapers toward the front end. The sperm cells of different animals vary greatly in shape but in most cases we notice a so-called "head" and a slender "tail."

Let us now follow fertilization in somewhat greater detail. (See Fig. 10.) The sperm cell has reached the egg, and is entering. The head has entered. The tail, having performed its function (that of locomotion) and being of no further value, sometimes breaks off and is left behind, outside of the egg. It is the "head" that is the really important part of the sperm cell. After it enters the egg we see in it changes which show the real character of the structure in question. For the "head" gradually approaches the nucleus of the egg and at the

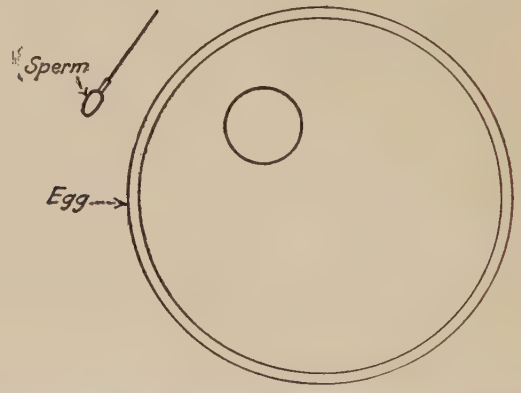

FIG. 9. Human sperm and egg cell both highly magnified.

same time becomes larger and spherical (probably by the taking on of water), and it becomes almost identical in appearance with the nucleus of the egg. We have no difficulty now in recognizing the structure under discussion: it is really the nucleus of the sperm cell,

and we shall now, instead of calling it the sperm cell "head," refer to it as the sperm nucleus. We also see why the sperm cell is regarded as a cell. Its "head" is nothing but a very condensed nucleus; its cytoplasm

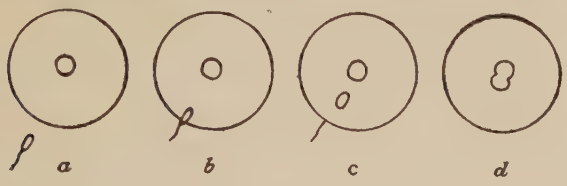

Fig. 10. Stages in fertilization.

is represented for the most part by the tail and a thin, clear layer of protoplasm enveloping the "head."

The sperm nucleus, having entered the egg, approaches the egg nucleus. The two unite to form a single nucleus and fertilization is complete. A new being is now launched into the world. He begins life as a fertilized egg and grows by a process of duplication and reduplication — cell division. He comes eventually to consist of billions of cells, but we can trace everything back to a single cell, the fertilized egg from which he began.

Now under the microscope, even its highest powers, the fertilized eggs of widely different animals look very much alike. In the egg of man we see a nucleus surrounded by clear cytoplasm; in the egg of the earthworm, we see very much the same thing. And still the fertilized eggs of man and of the earthworm must differ somehow in their make-up — they have such different possibilities of development. It must be remembered in this connection that there are a great many things which are too small to be seen under a microscope and

it is just these things that may have an important bearing on the specific character of the fertilized egg and its possibilities of development. This, in fact, is known to be the case. The developmental power of the egg has as its basis an organization which in large measure is too fine to be detected under the microscope.

The material that constitutes the fertilized human ovum is probably the most remarkable in the whole universe. Just think of it, in this microscopic speck are locked up all the remarkable possibilities, both physical and mental, of a human being!

There is much evidence to show that the nucleus determines the developmental possibilities of the egg. Among other things, it is known that a person gets his inheritance equally from both his parents, as witness the case of the mulatto. In skin color and in other ways he is intermediate between his parents, and presumably he has inherited as much from his father as from his mother. Still, you will recall that the father contributes, through the sperm cell, practically only a nucleus to the fertilized egg. The male parent is therefore resticted to the nucleus of a sperm cell in transmitting his hereditary materials to his offspring. There is much additional evidence derived from the study of inheritance proving that the nucleus is the vehicle of inheritance.

If the egg is remarkable in being much in little, what must we think of the sperm cell, a body that is incomparably smaller and yet contributes just as much to our inheritance as the egg cell. A two-gallon bottle would by no means be necessary to hold all the sperm cells that fertilized the eggs from which the present day

inhabitants of the globe developed. All of these sperm cells — containing the entire paternal inheritance of a billion and a half human beings — all of them could have been packed into a small space about twice the size of a pin head.[1]

[1] Based upon an estimate made by H. J. Muller.

CHAPTER II

INHERITANCE AS SEEN THROUGH THE MICROSCOPE

We must look to the nucleus for the structures which are concerned with inheritance. Now ordinarily there is no particular structure definitely visible in the nuclei of the sperm and egg cells. But it is known on indirect grounds that they contain rod-shaped bodies.

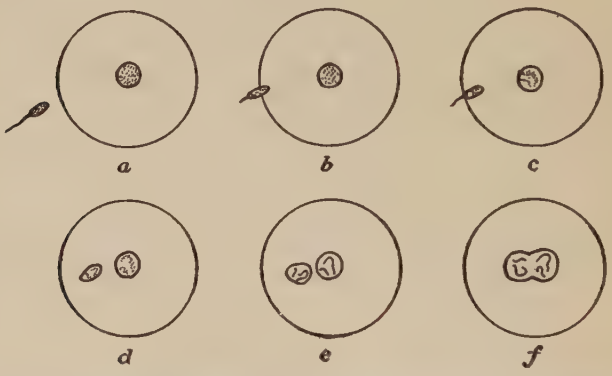

Fig. 11. Diagram of stages in fertilization to show the chromosomes. Only two chromosomes, instead of twenty-four, the figure for man, are shown coming from each sperm and egg nucleus.

It is these bodies that constitute our inheritance. They are known as the chromosomes (see Fig. 11). The sperm nucleus contains twenty-four of them, so does the egg nucleus; and the fertilized egg formed by the combination of the two contains forty-eight chromosomes. These are the figures for man. But all other species

of animals and plants contain chromosomes, though not necessarily the same number; and in all forms of life, they are the things that link one generation to the next and that cause the offspring to conform to their parents. In some manner, at present not understood, they determine the course of development; and in this way they cause us to resemble our parents. The fact that they come from both parents explains why we resemble either or both of them; and the further fact that the same number comes from both explains why each parent has an equal say in heredity. In brief, we begin life as a little bag of chromosomes — the fertilized egg. What happens to them in the course of development?

When the process of development begins and the fertilized egg prepares to divide into two cells, the chromosomes undergo an important change. Each of them splits lengthwise into two. While they are doing this they line up the middle of the cell and become connected with fibres that develop from opposite "poles" of the cell. (See Fig. 12*a* and *b*.) The split halves of each chromosome next pass to the opposite poles, drawn there, according to some biologists, by the contraction of the fibres. The cell now divides into two (see Fig. 12*c* and *d*).

The chromosomes in the new cells grow to their original sizes and they furnish the substance that constitutes the nuclei of these cells. When the new cells prepare in turn to divide, chromosomes again emerge from the nucleus. It is believed on very good grounds that they are the very same chromosomes that entered the nucleus. In brief, the chromosomes of the fertilized egg divide and form those of the first two cells. These

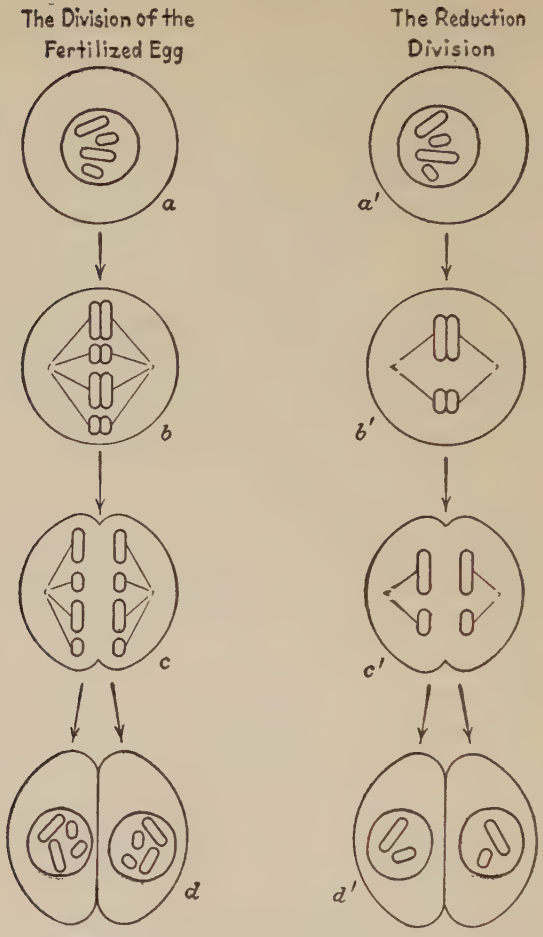

FIG. 12. Diagram showing how the chromosomes are distributed in cell division.

in turn divide and form those of the first four cells. By a repetition of this process, the chromosomes come to populate all the cells of the body. Note especially that they are all the "descendants" of the chromosomes originally present in the fertilized egg. Note too, that

their number, 48 for man, is maintained in every cell, so long as cell division is preceded by chromosome division; for one cell becomes two through division, and at the same time the one set of forty-eight chromosomes becomes two sets, one for each new cell.

What has just been said regarding chromosome number applies to ordinary cells, such as those of the brain, skin, muscles, etc. But the same rule does not apply to the reproductive cells. These particular cells have not 48, but 24 chromosomes. It is necessary that the reproductive cells should have the "reduced" number, as it is called, for if each had 48 chromosomes, like ordinary cells, then they would form by their union at the time of mating a fertilized egg having 48 plus 48, or 96 chromosomes and so there would be a doubling of the chromosome number in this and every later generation. But the chromosomes change in number from 48 to 24 in going to the reproductive cells.

The change is brought about through a special type of cell division, known as the reduction division, that takes place in the reproductive organs. In cells that undergo this particular type of division, the chromosomes do not first divide, as they ordinarily do, but they come together in pairs in the middle of the cell (see Fig. 12*a'* and *b'*). The members of each pair then separate to opposite poles of the cell, drawn there possibly by the fibres; and now the cell divides into two (see Fig. 12*c'* and *d'*). In this way the chromosome number is reduced from 48 to 24. Before the reduction division there are 24 pairs of chromosomes in each cell, or 48 in all. After this division there are just 24 unpaired chromosomes. It is

from these cells with the reduced chromosome number that the reproductive cells are derived in the male and the female. The cells formed by the reduction division do not develop directly into the reproductive cells. Instead, they undergo one further division, but without any further reduction in chromosome number (see Fig. 13). In other words, from any cell that undergoes the reduction division, four cells are eventually derived. In the testes all four develop into sperm cells.

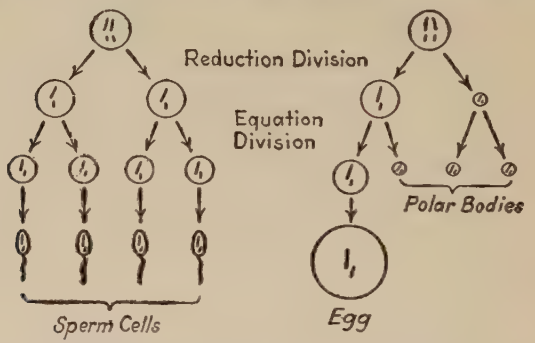

Fig. 13. Diagram of the "equation division," in both male and female, and of polar body formation, in the female.

In the ovary only one develops into an egg; the other three become functionless and stick to the side of the egg, forming small cells known as "polar bodies"(see Fig. 13).

Why the reduction division should be followed by another division and why the polar bodies should be formed in the female, are questions of detail that need not concern us here. The important thing is that the reproductive cells both of the male and the female have the reduced number of chromosomes, 24.

When fertilization takes place, the full number of

chromosomes (48) is again established; and it is maintained in all cells that are produced by the ordinary type of cell division ("mitosis" as it is sometimes called). Most cells of the body, including those of the skin, muscles, brain, etc., arise through ordinary cell division and contain the full number of chromosomes. The reproductive cells on the other hand contain the reduced number.

Our bodies contain myriads of cells, each with its chromosomes. But all of the chromosomes can trace their ancestry back to the original 48 in the fertilized egg. These in turn were derived from our parents. Our entire beings are therefore permeated with the microscopic bodies that form the material basis of inheritance and that cause us to conform to our parents.

We sometimes hear a person state that he inherited his blue eyes, or some other trait, from one of his parents. Strictly speaking, any such statement is incorrect. We do not inherit any traits from our parents. Blue eyes and other traits are not in the fertilized egg. All we inherit is chromosomes. During the course of development traits make their appearance. The particular traits that develop are determined in general by the particular kind of chromosomes that we inherit.

But we must not overlook the environment. It too influences development. Witness the difference in the growth of a well nourished child and one who is poorly nourished. Or take the case of mental development. Everybody knows how great is the extent to which training and environment in general influence a person's ability. There are some people who go so far as to say that there is no such thing as heredity; mental ability,

they assert, is entirely a matter of environment — getting a good start and coming under the right influences. This viewpoint implies that everybody is born with exactly the same inherent ability, and that all differences that later appear are entirely due to environment.

Many of the mental differences that we observe between human beings undoubtedly have no heredity basis at all. The children of a bank president or of a college professor may follow in the footsteps of their father largely because of their home environment and not because of special kinds of chromosomes that favor the one type or the other in development. Even temperamental differences such as we notice between different races may have very little heredity basis; witness the speed with which foreigners become "Americanized" and lose their marked peculiarities once they are in the same social environment. We must, therefore, be very cautious in referring special mental traits to heredity.

At the same time, it would be very odd if such a complicated organ as the brain were exactly alike in everybody by nature. Every organ of the body, the brain included, is probably subject to heredity variations. Take the eyes. Some people are born with blue eyes, others with brown; and there can be very little doubt that each of these traits has a special heredity basis. But in the case of the brain and the mind, it is difficult to determine which of the differences that we see between people are due to heredity, and which to environment. Most physical traits are like the eyes in the relative fixity of their development. If you knew that a fertilized egg had the chromosomal basis for blue eyes,

you could be reasonably sure that it would develop into a blue-eyed person, not brown. Had the chromosomes been for some mental trait, say mathematical ability, then you could not be so sure as to what would happen. You would have to consider the special environment in which the person developed because anyone might appear very stupid at mathematics if he had the wrong training along these lines, even though he had the right heredity. In this respect the mental trait in question is different from a physical trait, such as blue eyes.

But you could not reasonably conclude on this account that blue eyes were entirely a matter of heredity and mathematical ability entirely a matter of environment. Each trait requires both heredity and environment for its development. It so happens, however, that the normal environment supplies all the conditions necessary for blue eyes, possibly because this trait develops in large measure while the embryo is in the uterus of the mother, where the relatively few conditions necessary for its development are sure to be found. The conditions that influence the development of a mental trait are on the other hand extremely numerous. They come into play during the entire mental development of a person and appear in the most diversified forms in his environment. They would not be likely to be the same for any two persons. As a result a mental trait shows a good deal of variation.

One way to decide what parts heredity and environment play in mental development would be to raise children under conditions that were exactly the same for all, or as nearly so as reasonably possible. If now, all the children should not develop the same ability,

then the differences would have to be due to heredity. Those with exceptional ability would have chromosomes of a characteristic type. But even if they should all develop alike, their mental ability would still have a heredity basis, only it would be the same for all people. In other words everybody would have exactly the same kind of chromosomes for mental ability. Unless chromosomes had something to do with mental development, then an ape raised among humans would develop human intelligence. If, now, the chromosomes at the basis of mental development were exactly alike in all human beings, then the particular extent to which their mentality developed would be a matter of environment and exceptional ability would have no *special* hereditary basis. The question, "Which is more important, heredity or environment?", raises a problem which really has no answer. It puts us in the same sort of difficulty as if someone wanted to know whether a fish's tail or the water in which he swims is more important for his swimming. Obviously both are absolutely necessary and neither can be said to be more important than the other. So with heredity and environment. The fertilized egg could not develop without its chromosomes, neither could it develop if it were removed from the womb of the mother and deprived of the proper nourishment, warmth and other environmental conditions. At the same time it is true that some traits are more easily influenced by environmental conditions than others.

The student of heredity must as a rule deal with traits that are rather fixed in their development in order that he may not be confused by the effects of environment.

He wants to know what kind of chromosomes parents transmit to their offspring and how they transmit them. The study of these processes, in fact, constitutes the science of heredity. But the chromosomes are ordinarily hidden from view; and they manifest themselves to us only through the influence they have on development. It is therefore necessary in heredity to work with definite physical traits. But once we understand the hereditary basis of physical traits, we are prepared to go to mental traits and understand and control them.

CHAPTER III

INHERITANCE AS SEEN THROUGH THE BREEDING PROCESS—THE MENDELIAN DISCOVERY

The year 1822 was an eventful one in the annals of biology. In this year, there were born Pasteur and Mendel. Pasteur's discoveries revolutionized medicine and surgery. To-day, everybody knows of the relation of germs to infectious diseases. The name of this biologist has become a household word. Mendel's discoveries revolutionized the science of heredity. Their ramifications into human welfare were not so apparent as those of Pasteur, and yet it is entirely possible that eventually the laws of Mendel will be as momentous in their bearing on human progress as were the discoveries of Pasteur.

Mendel performed his experiments in the spirit of pure science. He crossed different varieties of peas and produced hybrids. He was not particularly interested in improving the varieties of peas by his hybridization experiments. Instead, he had in mind the hybridization process itself.

It had been long known previous to Mendel's time that a hybrid might have offspring of varied type. But no exact relationship had been established between the parents of a hybrid and its offspring; nor was attention focussed upon some particular and simple character

by which the parents of the hybrid differed, and the way in which the character appeared among the offspring of the hybrid. This was left for Mendel; and his method changed the study of heredity from chaos to an exact science.

Mendel crossed various types of peas which differed in regard to flower color, texture and color of seed, etc. For example, he produced a hybrid by crossing a yellow-seeded variety with a green-seeded variety; and then he followed the distribution of these characters among the offspring of the hybrid. He found, in short, that the characters which appeared in the parents of a hybrid, reappeared again among the offspring of the hybrid. There was a definite ratio in which these characters were distributed among the offspring; in this particular case, there were 3 yellow to 1 green. The hybrid itself was yellow, and showed no outward evidence of green. But it carried the hereditary stuff of the green parent, side by side with that of the yellow parent. This was shown by the fact that green, as well as yellow offspring were produced by the hybrid parent.

Mendel grew another generation of plants from the offspring of the hybrids, in order to find out more about their hereditary make-up. He found that the green plants produced nothing but green offspring. They were pure green, like the original green parent. The yellow, on the other hand, were of two kinds. One out of every three produced nothing but yellows. They were pure yellow. The remaining two produced both yellow and green, just as did their hybrid parents, and like them, were hybrids. In brief, the hybrid parents

produced pure yellows, hybrids, and pure greens in the ratio of 1 : 2 : 1. But the pure yellows and the hybrids looked alike and when the offspring were classified according to their outward appearance, they gave a ratio of 3 yellows to 1 green.

Mendel observed one very important fact in his experiments, namely that the hybrids produced pure yellow and pure green offspring, and these were just as pure as the original parents. It followed not only that the yellow and green units existed side by side in the hybrid, but also that these units did not mix with each other. Had they done so, it would have been impossible to recover the pure types from the hybrids. The hereditary units must have remained distinct. This in fact, was the essential result of Mendel's experiments — the non-miscibility in a hybrid of certain hereditary stuffs derived from the parents.

The appearance of the hybrid is a matter for further consideration. The plant which carries the green as well as the yellow unit shows no evidence of the green; it looks like a pure yellow. The green unit does not express itself in the presence of the yellow unit and is said to be recessive to yellow, which in turn is said to be dominant to green.

The rule of dominance and recessiveness holds in many cases, but not in all. Thus, a more recent plant breeder,[1] following Mendel, crossed two races of plants known as "four-o'clocks," one with red flowers, the other with white. The hybrids had pink flowers. Here the rule of dominance does not hold.

It also seems at first sight as though the red and white

[1] Correns.

units mixed with each other in the four-o'clocks and became pink. To find out whether this is really the case, we must get the offspring of the hybrids. If the units have really become mixed, then the hybrids can produce nothing but pink offspring. But if the red and white units have remained separate, then the hybrids can produce some pure red offspring and some pure white. This in fact, is found to be the case. In addition to the pure red and pure white offspring, the hybrids produce some offspring that are pink. But these pink offspring again are hybrids. They in turn are capable of producing pure red and pure white offspring. The hybrids, in brief, appear pink, but they contain the color units in pure form.

The color of the hybrid four-o'clocks might be compared to the pink light which would result if lights from red and white lamps were thrown on a screen at the same time. In this case, there is no mixing at the source; the red and white lamps are themselves not changed. In the same way, the red and white units in the four-o'clock give rise to a mixed expression, but the units themselves do not mix; otherwise the hybrid could not produce pure red and pure white offspring.

The ratio which Mendel got can be readily explained. When the hybrid forms its reproductive cells, the yellow and the green units separate from each other. One half of the reproductive cells receive the yellow unit, one half the green. When two "yellows" come together, we get a pure yellow offspring. When two "greens" come together, we get a pure green. When a yellow and a green, or a green and a yellow come together, we get a hybrid. The combination that pro-

duces the hybrid occurs, as a mere matter of chance, twice as often as either of the other two. We get accordingly the 1 : 2 : 1 ratio.

Mendel found that hybrids of other kinds produced offspring in accordance with the same principle as did the yellow-green hybrid. For example he crossed a race of peas that has a smooth seed coat with another race that has a wrinkled seed coat. When Mendel did this, he produced hybrids with smooth seed coats; and from the hybrids he got offspring of two types, smooth and wrinkled in the ratio of 3 : 1.

Mendel carried his work further. He found in his hybridization experiments that it was possible to bring together traits that were in separate races, and to separate from each other traits that were previously together in the same race; and that all sorts of combinations could be made between the traits of one race and those of the other.

Let us consider a case of this sort that Mendel worked out. He crossed a race that was smooth and yellow to one that was wrinkled and green. The hybrid appeared smooth and yellow (see Fig. 13*a*), but it also carried the recessive units for wrinkled and green. The hybrid now produced offspring of several types. Some of them were like the original parents, smooth and yellow, or wrinkled and green. But others had a new combination of traits, the smooth seed coat of the one parent and the green color of the other; or the wrinkled seed coat and the yellow color. Mendel found that these four types were produced in a definite ratio, 9 smooth, yellow : 3 smooth, green : 3 wrinkled, yellow : 1 wrinkled, green.

Add up all the smooth and all the wrinkled in the ratio just given, and note that you get 12 smooth: 4 wrinkled, which is the same as 3 smooth : 1 wrinkled. Also, add up all the yellows and all the greens, divide through, and you get a ratio of 3 yellow : 1 green, again the simple Mendelian ratio. The offspring of the hybrid fall into the simple Mendelian ratio when either trait (coat texture or coat color) is considered by itself. But when you classify the offspring for both traits at the same time, you get the 9 : 3 : 3 : 1 ratio.

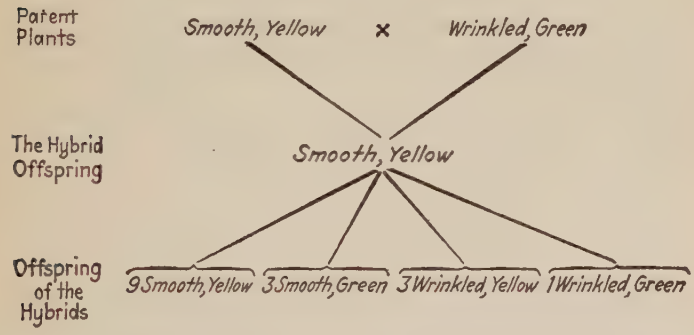

FIG. 13*a*. Diagram to show how traits may be shuffled through the breeding process. Compare the parents of the hybrids with their offspring.

In any event, the hybrid produces offspring with all four possible combinations of coat texture and coat color. Such an assortment could be possible only if the hereditary units for these traits were separable from each other in the hybrid. Thus Mendel showed that the hereditary make-up of the plant consisted of separable units. These units we now refer to as "genes."

Mendel's principle has been found to apply to a large number of lower animals and plants, and also to man. Idiocy is an example of a human trait that has a simple

Mendelian hereditary basis. The reproductive cells of an idiot all contain a gene or hereditary unit that we can designate by the letter "*f*" (the gene for feeble-mindedness). The reproductive cells of a normal person all contain, instead of the idiot gene, a normal gene that we can designate by the letter "*F*." If an idiot should mate with the normal person, a fertilized egg of composition $\frac{f}{F}$ would be formed; for *f* would come from the idiot parent, and F from the normal parent. This fertilized egg would develop into a perfectly normal appearing person, because the normal gene (*F*) is dominant to the one for feeble-mindedness (*f*). Such a normal appearing person is however, a hybrid, and he is different in his hereditary make-up from a pure normal $\left(\frac{F}{F}\right)$.

If two hybrids mate $\left(\frac{F}{f}\times\frac{F}{f}\right)$, they might have idiot children. For half the egg cells of the mother and half the sperm cells of the father have the gene for feeble-mindedness (*f*) and when two such reproductive cells come together, a fertilized egg is formed of composition $\frac{f}{f}$. This develops into an idiot child. Normal children would also be expected in the family, for only half the reproductive cells of the parents are *f*-containing; the other half have the normal gene (*F*), and they might produce either pure normal offspring $\left(\frac{F}{F}\right)$ by combining with each other, or hybrids $\left(\frac{F}{f}\right)$ by com-

bining with the reproductive cells that contain *f*. That is to say, there are in all three classes of offspring expected when two hybrids mate, namely pure normals $\left(\frac{F}{F}\right)$, hybrids $\left(\frac{F}{f}\right)$ and idiots $\left(\frac{f}{f}\right)$ and they are expected in the simple Mendelian ratio of 1 : 2 : 1, respectively. Or, if we combine the first two terms of this ratio by adding together the pure normals and the normal appearing hybrids we get on the average 3 normal children to 1 idiot in a family when both parents are hybrids.

This ratio, bear in mind, is purely an average result. If two hybrids had just four children, it would by no means follow that 3 would be normals and 1 an idiot. Two or more of them might be idiots because there might, as a mere matter of chance, be a "run" of this particular class. The combination of the reproductive cells in fertilization is entirely a chance process, and the particular combination that produces the idiots ($f \times f$) might occur more often than expected on the average when you are dealing with a small family. On the other hand, all four of the children might very well be normal, because the particular combination of reproductive cells necessary for the production of the idiot might not have occurred at all, just as a matter of chance. In a small family especially, of just two or three children, all might be normal appearing and nobody would suspect that there was any idiocy in the family. One or more of the children might, however, very well be hybrids, and these could transmit the idiot gene to future generations.

The hybrids would, as a matter of chance, probably not marry other hybrids like themselves, but pure

normals $\left(\frac{F}{F}\right)$ which are more abundant in the population at large. The children from these matings $\left(\frac{f}{F} \times \frac{F}{F}\right)$ would all appear normal. But half of them, on the average, would again be hybrids $\left(\frac{f}{F}\right)$ for the simple reason that half the reproductive cells of the hybrid parent contain *f*. The family might therefore very well carry the idiot gene for many generations without its showing. If however, this family should by chance marry into some other family which also had been carrying the idiot gene, then feeble-minded children might turn up. Their appearance would seem very strange and unexpected, because each family would claim that there was no evidence of idiocy in their stock. But if the two families had complete family records and should trace their ancestry back far enough, each would probably find that it had an idiot ancestor in some part of its family tree. This idiot was of composition $\frac{f}{f}$; that is, pure for the feeble-minded gene. He or she probably mated with a pure normal $\left(\frac{F}{F}\right)$ and so the hybrids $\left(\frac{F}{f}\right)$ came into existence. These then continued to transmit the idiot gene, possibly for many generations, during all of which time it could never manifest itself, because it was prevented from so doing by the dominant normal gene. When, however, the idiot gene from one family came together with the idiot gene from another it could again manifest itself.

Animal breeders, before the days of Mendel, had

observed in animals the sort of thing just described for man. In a given stock there would suddenly crop up a trait which had at some previous time been observed in the stock but which had remained dormant for many generations. Breeders referred to this as a "reversion," or "atavism." In the light of the Mendelian discovery, we know the explanation of such "reversions."

You have perhaps heard of two brilliant people having an idiot child, and of the suggestion that the idiot was the result of an "hereditary reaction" that followed upon several generations of over-development. No such view has the slightest evidence in its favor. The parents, in spite of their brilliance may very well have been hybrids, and probably were. Many people are hybrids without they themselves or anybody else suspecting it. In fact, according to a certain calculation, about one person out of every ten is hybrid for feeble-mindedness. The calculation in question may possibly be subject to error, but even at that it seems fairly certain that there are a very large number of hybrids in existence, many more than is generally supposed. What is more, these hybrids, as well as the outright idiots, seem to be on the increase.

The cause for the increase is not to be found in any unusual set of circumstances in our present-day environment. It is due to just one thing — the disproportionate rate of reproduction of the feeble-minded. The total number of idiot genes is actually being increased through reproduction and passed on to the population at large. Here they remain concealed from view in the hybrids, but ready to manifest themselves again whenever the hybrids happen to mate.

Other traits in man, besides feeble-mindedness, have been found to appear in the simple Mendelian ratio among the children of hybrid parents. In the list are included eye color (blue as a rule being recessive to brown), hair color (red being recessive to other colors, not-red), fatness (recessive to the normal condition), webbed hands (recessive to the normal condition) and three other hand defects; namely, brachydactyly (short stubby fingers, due to the absence of a joint), polydactyly (extra finger) and "lobster claw" (a splitting of the hand down its middle), all three of them dominants. Included in the list is also white forelock (a splash of white hair, sometimes called "blaze," a dominant).

A rather unusual case is that of baldness, which seems to be recessive in women, and dominant in men. This means that it takes two "doses" of the "bald" gene to make a female bald, but only one to make a male bald. The reason for the greater prevalence of baldness among men is obvious. A case of a similar sort has been well worked out in sheep, in which it has been found that the horns of a certain breed are a dominant trait in the males, recessive in the females. When sheep are bred that are hybrid for the trait, they produce male offspring in the ratio of 3 horned: 1 hornless, but females in the ratio of 3 hornless : 1 horned.

Whether or not a trait is a dominant or a recessive in man is sometimes not so easy to decide by a mere count of offspring in a given family. Take for example feeble-mindedness. Suppose that nobody had told you this was a recessive but that you had observed a family of

say four children, and had found two of them feeble-minded, two normal. This ratio, half normal and half feeble-minded, you now know is one that you would get on the average if one parent were an idiot and the other a hybrid, with idiocy as a recessive. But you would expect the same ratio if idiocy were a dominant, and if further the idiot parent were hybrid. This would make the normal gene recessive, and the normal parent would be pure for it. You could therefore not jump to the conclusion that idiocy was a recessive merely on the basis of what you had observed of the family in question. Suppose though, that you studied other families, and noticed that the offspring of two idiots were never anything but idiots. You could then conclude that idiocy was probably a recessive, for if it were a dominant, two idiot parents might sometimes be hybrids, and they could therefore have both normal and idiot children. But if it were a recessive, the idiots could not be hybrids; they would always have to be pure for the idiot gene, and two such parents could never have anything else but idiot children.

You could also get valuable information from the married brothers or sisters of the idiot parent. If none of them had idiot children, you would be lead to suspect that the idiot gene was a recessive; for the brothers and sisters of the idiot might very well also carry the idiot gene and transmit it to at least some of their children. If none of them grew up as idiots you could be fairly sure that the idiot gene was recessive to the normal gene. On the other hand, if several of these brothers and sisters had idiot children, you would be lead to suspect that the idiot gene was a dominant,

especially if they had married into unrelated families; for it would be rather unlikely that all these other families should also carry the idiot gene.

There is also that skipping of a number of generations in the appearance of the trait, made possible by the fact that it can be carried in a hidden condition by the hybrid. Such a possibility applies only to a recessive trait. A dominant, if carried at all, whether in the hybrid or the pure type, would manifest itself. No generation that carried the gene for the trait could fail to show it. When we find therefore that idiocy does sometimes skip a number of generations in making its appearance, we can be fairly certain that it is a recessive trait.

Consider now, how much easier the student of heredity finds his task when he is dealing, not with human beings, but with lower animals and plants. Say he was dealing with an insect. He would find two races that had some distinct difference, cross them, and get the progeny from the cross. These would be the hybrids (or F_1, as they are sometimes called). He would next inbreed the hybrids and get their progeny (F_2). From a single couple, he might get as many as two to three hundred offspring; and if there were anything like a 3 : 1 ratio among them, there would be no difficulty in detecting it or in telling which trait was recessive. Plants are also serviceable for such studies because they produce seeds in large numbers. On the other hand, the student of heredity finds human material very unsuited to his purposes. He must be able to control his crosses and get large numbers of progeny from his hybrids. For these reasons, comparatively little prog-

ress has been made with human heredity; and it would indeed have been almost impossible ever to arrive at Mendel's law if we had confined ourselves to man. But nevertheless man is an extremely important animal; in fact, the science of heredity, as well as every other science, can justify its existence only in so far as it ultimately contributes to an understanding of man himself and to his welfare and happiness. Now that the tracks have been cleared by the lower forms of life, we are better prepared to study ourselves.

CHAPTER IV

BREEDER AND MICROSCOPIC WORKER JOIN HANDS

Mendel knew that the hereditary units were transmitted from parents to offspring by the reproductive cells, but he did not know exactly in what part of the cell they were located. Some discoveries have recently been made which tell us that the units of heredity are carried by the chromosomes, the rod-shaped bodies that are contained within the nucleus of the cell.

The discoveries in connection with the chromosomes were made largely by a small group of American biologists who used as their experimental material the fruit fly (Drosophila, see Fig. 14). You have probably seen these small insects hovering about fruit stands without taking particular notice of them, and you might very well be surprised that anybody should spend his time breeding them. Still, these creatures proved to be very favorable material for experiments in heredity. All that was necessary in breeding them, was to put a couple of them in a milk bottle with a little banana for food, and in about ten days the bottle (properly stoppered with cotton) would be swarming with offspring.

The researches on the fruit fly produced a wealth of information regarding the hereditary make-up of the animal, and led to conclusions that have been found to apply in a general way not only to the fruit fly itself,

but to other animals and plants, and probably even to man. These researches showed that the hereditary units — the genes, as we now call them — are located in the chromosomes, arranged in a line along their length. It was found that practically every trait of the fruit fly, such as its wings, its eye color etc., was influenced in its development by numerous genes, located at definite points in the animal's chromosomes. No less than a

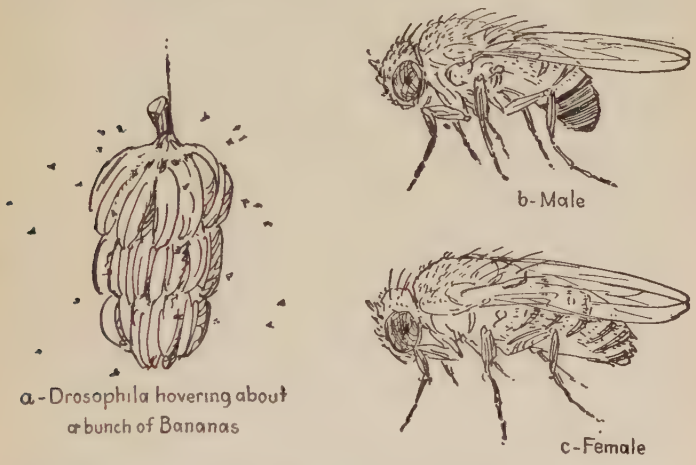

FIG. 14. The fruit fly (Drosophila). Many of the recent discoveries in heredity were made on this animal.

dozen genes were discovered that influenced eye color, another group that influenced wing development, etc. The genes that made for eye color were not found to be bunched together in one chromosome and those that made for wings or some other trait in another chromosome. On the contrary those for any one trait were scattered quite at random among all the chromosomes, and they were mingled with those for other traits. An eye color gene might be next to a body color gene in

one chromosome, but in another chromosome, or in some other part of the same one, an eye color gene might be next to one for wings. In brief, there was found to be positively no relationship between the organ that a gene influences and the position of the gene in a chromosome. Any gene does, however, occupy a definite position in a chromosome, from which it does not wander. This position is referred to as its locus. Genes at different loci are presumably not alike, even those that influence the same organ.

Just how all of this is known, is a long story. Bear in mind that the genes are too small for us to see under the microscope, and that even if our microscopes were powerful enough to disclose them to the eye, probably all that we would see would be particles of protoplasm all of which appeared more or less alike; and we could not say that this one was for eye color, that one for wings, etc. It required a long and carefully conducted series of experiments to find out in the first place that the genes were in the chromosomes. Then the location of any particular gene had to be determined by special experiments. By no means all of the genes that Drosophila possesses have been located, and probably never will be. It is believed that a single chromosome has possibly several thousand genes.

While Drosophila was kept under observation in the laboratory, new races occasionally made their appearance. One of these races had very short wings, mere stumps, and was called "vestigial." The ancestors of the vestigial race were at one time ordinary normal flies with long wings, but in one of these normal ancestors a change occurred in a certain gene that had to do with

wing development. The change was referred to as a "mutation." It occurred at a certain locus in a certain chromosome, known as the "second" chromosome. None of the other "wing" genes were affected by the mutation; they remained the same as in the normal long-winged race. Mutations had, however, taken place on different occasions at other "wing" loci, and these

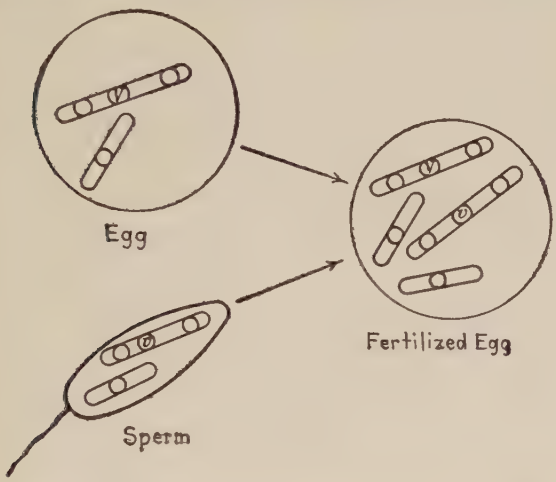

FIG. 15. Diagram to show the chromosomes and genes in a cross between a long-winged female and a "vestigial" male. Not all the chromosomes or genes are shown.

produced races with other wing abnormalities, such as "bent," "rough margins," etc. The normal development of the wings depended apparently upon the presence of normal genes at all the wing loci. In the mutant races there was lacking at one locus or another, some gene necessary for normal wing development, and in its place was some other type of gene that arose by mutation from the normal gene. No one of the normal genes by itself produced normal wings; they simply produced

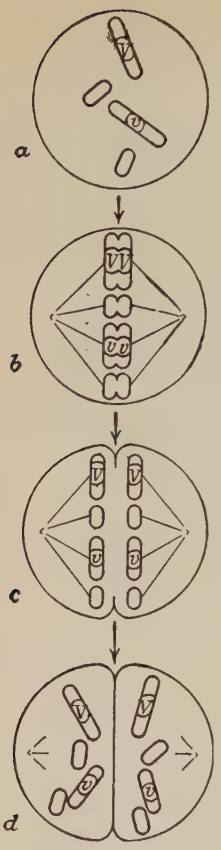

FIG. 16. Diagram to show the division of the fertilized egg $\frac{V}{v}$. The diagram includes only two pairs of chromosomes and the genes *V*, *v*.

normal wings through their combined effects in development. But when any one of them changed by mutation, there was a corresponding abnormality in wing development in the race that had the mutated gene.

Compare now a mutant race, say "vestigial," with the normal as regards their chromosomes and genes (see Fig. 15). The reproductive cells of a vestigial fly (either a male or a female) have the same kind of chromosomes as an ordinary fly; and they have the same kind of genes, excepting at the "vestigial" locus where the mutated gene (*v*) is. In the normal fly, this particular locus is occupied by one of the normal genes. It would not do simply to call this *the* normal gene because we should imply that there were not also normal genes at other loci. So let us simply call the normal gene in question "not-vestigial," and designate it by *V*. The normal genes at other loci are the same in both the vestigial and the normal races, and we need not be especially concerned with them for the present.

The vestigial race was crossed to the normal race and hybrid offspring produced. The hybrids appeared normal. Let us see what their chromosomes and genes were

like. Consider a cross of vestigial male by a normal female and omit, for the sake of convenience, all chromosomes but the one with the vestigial locus (designated by Drosophila workers as the "second" chromosome) and one other chromosome (designated as the "third") to represent the other chromosomes. Remember that all the chromosomes, four in number, are really present in the reproductive cells and are transmitted from the parents to the offspring. The fertilized egg, produced by the cross, receives "vestigial" from the male parent and "not-vestigial" from the female. It receives in addition all the other "wing" genes, but they are the normal ones.

Note now, that the chromosomes are paired and that there are a couple of genes at each locus. The two genes at a given locus are referred to as allelomorphs. At most loci, the two allelomorphs are alike (as those not labelled in Fig. 15) and at these loci the fly is pure (or "homozygous", to use the technical term). But at the "vestigial" locus the allelomorphs are unlike, and at this particular locus the fly is hybrid (or "heterozygous").

The fertilized egg develops into the adult, and in so doing it gives rise to numerous cells, each with its chromosomes and genes. Most of these cells arise through ordinary cell-division and have chromosomes that are exactly like those of the fertilized egg in that their chromosomes are paired. But in the reproductive cells, the chromosomes are unpaired. The same thing is true of the genes. An "ordinary" cell contains both allelomorphs at any locus; a reproductive cell contains just one or the other.

Note now, just how the reproductive cells come to

differ from the ordinary cell. Consider first the fertilized egg. When it prepares to divide the chromosomes line up in the middle of the cell and divide (see Fig. 16). This applies to both members of each pair of chromosomes. The halves of each chromosome are then drawn to opposite poles and the cell constricts into two. Each new cell is now just like the fertilized egg, with paired chromosomes and paired genes. The two cells produce 4 cells by division; and all four of the new cells have paired chromosomes and genes. The four produce eight, and so on, until a large mass of cells is formed, all just like the fertilized egg with paired chromosomes and paired allelomorphs. All the cells resemble the fertilized egg because they all arose from the fertilized egg through the "ordinary" process of cell-division (mitosis, as it is called).

The type of division just described is the usual type. But in the reproductive organs another type takes place — the reduction division. At this particular division, the chromosomes come together in pairs in the middle of the cell; they do not line up and divide (see Fig. 17). The members of each pair are drawn to opposite poles of the cell, and they are separated by the division.

Note now that the allelomorphs have become separated, vestigial from not-vestigial, as well as the allelomorphs at all other loci. When the reproductive cells develop they contain only one allelomorph or the other at any locus, not both. Half of them contain vestigial, the other half not-vestigial. This numerical relationship follows from the simple fact that the reduction division forms the two types of cells in equal numbers.

Consider now what happens when two hybrids mate. Their reproductive cells come together, the sperm cells of the male and the egg cells of the female, and they form the offspring. But the sperm cells are a mixture

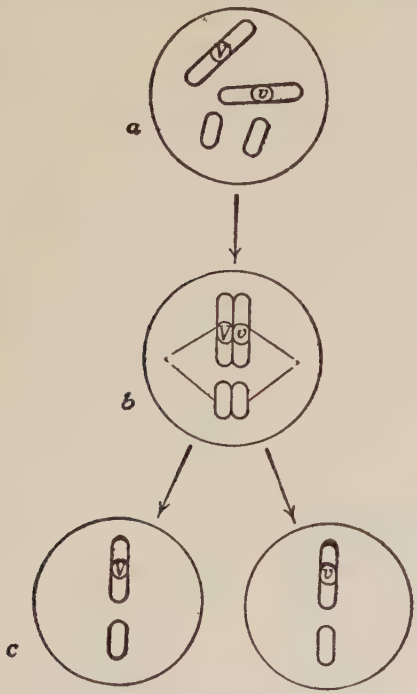

FIG. 17. Diagram of the reduction division in the $\frac{V}{v}$ hybrid.

of two types, vestigial and not-vestigial, and it is a mere matter of chance which of them will fertilize a given egg. Moreover, it is also a matter of chance whether this egg itself contains vestigial, or not-vestigial. If the two reproductive cells happen to be of like type (both vestigial, or both not-vestigial) we get a fer-

tilized egg of pure type $\left(\frac{V}{V} \text{ or } \frac{v}{v}\right)$, see Fig. 18; if they are not, we get a hybrid $\left(\frac{v}{V}\right)$. The combinations that produce the hybrid occur on the average, twice as often as either that form the pures, so that we get 1 $\frac{V}{V}$ pure normal) : 2 $\frac{v}{V}$ (hybrids) : 1 V (vestigial, pure).

You can readily arrive at the above ratio by first taking one type of sperm cell (say not-vestigial) with both types of eggs, and then doing the same for the

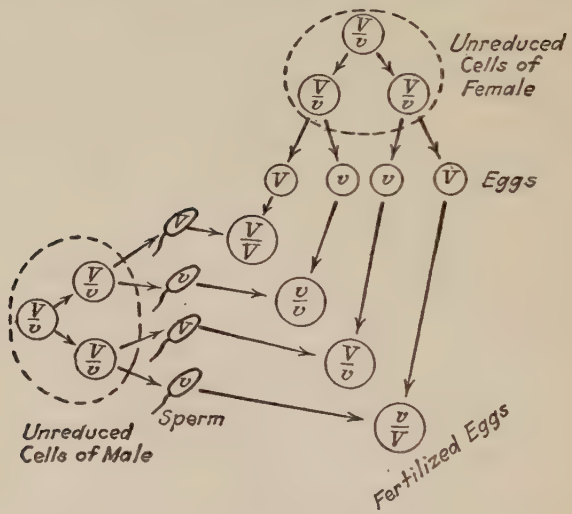

Fig. 18. Diagram to show how the reproductive cells are produced and how they combine when two hybrids mate $\left(\frac{V}{v} \times \frac{V}{v}\right)$.

other type of sperm cell (see Fig. 19). Thus we get the simple 1 : 2 : 1 Mendelian ratio; or, if we combine the pure normals and the hybrids (which also appear normal) we get the 3 : 1 ratio.

Other mutant races of Drosophila, besides vestigial, were crossed to the normal type. These crosses also gave the 3 : 1 ratio in the second generation. For example, a pink-eyed race was crossed to the ordinary

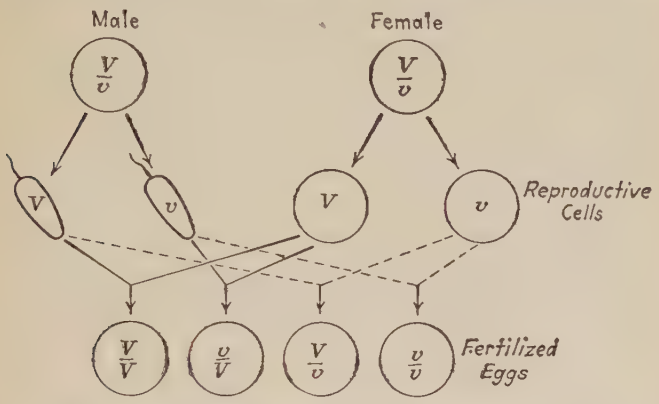

FIG. 19. Another way of representing the cross $\frac{V}{v} \times \frac{V}{v}$.

red-eyed race. The hybrids of the first generation were all of them red-eyed (red being dominant). When the hybrids were mated to each other they produced in the next generation 3 reds to 1 pink.

The explanation of the 3 : 1 ratio just given is the same as the one previously given for the vestigial-normal cross. The pink-eyed race has a gene (pink) at a certain locus in one of its chromosomes (the 3rd): the red-eyed race has the allelomorphic gene, not-pink, at the same locus. The cross produces a hybrid with a pair of 3rd chromosomes, one containing *p* (pink), the other *P* (not-pink). When the reduction divisions occur in the hybrids the chromosomes separate from each other. For this reason one-half of the reproductive cells receive *P*, the other half *p*. When the hybrids

mate, the reproductive cells come together in their various possible combinations and produce offspring in the ratio of $1\frac{P}{P} : 2\frac{P}{p} : 1\frac{P}{p}$, or 3 normal (red-eyed) : 1 pink.

Note that the results are not affected by the fact that the third chromosome pair (rather than the second) is involved in the cross. Flies that are hybrid at any one

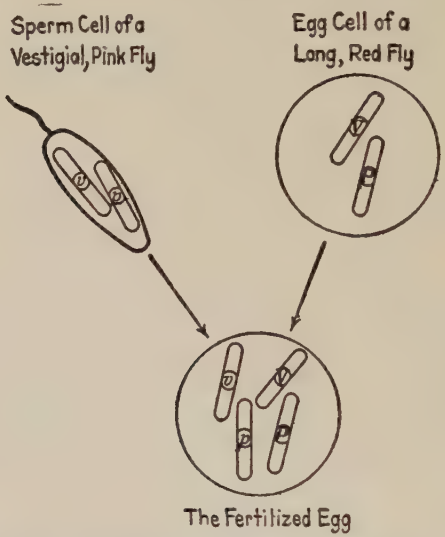

FIG. 19*a*. Diagram to show how the hybrid receives its chromosomes and genes when a vestigial, pink fly is crossed to a long, red fly.

locus, whether this happens to be a locus in the second pair, the third, or any other, produce offspring in the simple Mendelian ratio. The two chromosomes that form a pair are "homologous," and homologous chromosomes always separate at the reduction division. They make their way to different reproductive cells in equal proportions. It is for this reason that we get a 3 : 1 ratio when the hybrids mate and produce offspring.

It was found possible, through the proper experiments, to obtain flies that had both vestigial wings and pink eyes. The reproductive cells of such flies have vestigial (*v*) in their second chromosome, and pink (*p*) in their third. The normal race has instead "not-vestigial" (*V*) and "not-pink" (*P*). When the two races are crossed hybrid offspring are formed (see Fig. 19*a*). In making the cross we can use the male of either race and the female of the other. The offspring are hybrid at two loci. At the vestigial locus they have *V* in one of their chromosomes, *v* in the other. At the pink locus they have *P* in one of their third chromosomes, *p* in the other. The composition of the hybrids is represented in symbols as $\frac{V}{v}\,\frac{P}{p}$. These hybrids appear perfectly normal, because the gene not-vestigial (*V*) is dominant to vestigial (*v*) and makes the flies long-winged; and "not-pink" (*P*) is dominant to pink (*p*) and makes the flies red-eyed. The hybrids therefore have the appearance of the ordinary wild flies that are pure for the normal genes *V* and *P*, and that have long wings and red eyes.

When the hybrids are mated to each other they produce offspring of various types. Some of the offspring are like their normal grandparent and have long wings and red eyes. Others have vestigial wings and pink eyes like the other grandparent. Still others have the wing character of one grandparent and the eye color of the other. There are two possibilities here: a fly may have the long wings of the one race and pink eyes of the other, or it may have the red eyes of the first race and the short wings of the second. There are in

brief, four kinds of offspring in all, (1) long, red and (2) vestigial, pink (the two old combinations); (3) long, pink and (4) short, red (the two new combinations). These four types of offspring are produced in different proportions. If we arrange them in a certain order, after we count them up and classify them, we find that we get the familiar 9 : 3 : 3 : 1 ratio previously observed by Mendel in his peas; for there are, on the average 9 long, red : 3 long, pink : 3 vestigial, red : 1 vestigial, pink.

The chromosomes again tell us why the hybrids just referred to produce offspring in the 9 : 3 : 3 : 1 ratio. Let us see just how. The fertilized egg contains its chromosomes in pairs and so do all cells derived from it through the ordinary process of cell division. These cells all agree in containing both allelomorphs at the vestigial and pink loci. But before the reproductive cells are formed, the reduction division takes place and the allelomorphs separate from each other (see Fig. 20). This they do because the chromosomes containing them separate at the reduction division. Previous to their separation they always come together in pairs, the two second chromosomes containing vestigial and not-vestigial, and the two third containing pink and not-pink.

But note now two possible ways that the pairs may be arranged with regard to each other when they come together in the middle of the cell. The two chromosomes with the vestigial and pink units may line up to one side of the middle, and the two with not-vestigial and not-pink may line up on the other side. On the other hand, the two chromosomes with not-vestigial and pink

may line up on one side, and the two with vestigial and not-pink on the other side. Each type of reduction division produces two kinds of cells, or four in all, containing respectively (1) not-vestigial, not-pink, and (2) vestigial, pink, from one type of reduction division; (3) not-vestigial, pink, and (4) vestigial, not-pink, from

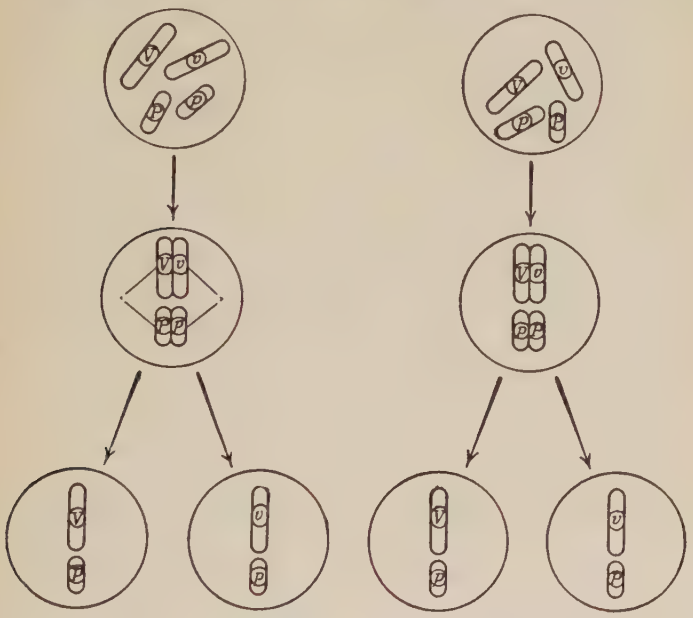

Fig. 20. The reduction divisions in a $\frac{V}{v}\ \frac{P}{p}$ hybrid.

the other type. From these cells the reproductive cells of the hybrid are derived. The hybrids are now ready to reproduce offspring.

A hybrid, it will be seen is somewhat like a laundry. You send a collar and a shirt to it; so does some one else. You may get back your collar and your shirt, and he his; but you are just as likely to get back your collar

and his shirt, and he his collar and your shirt. The laundry, however, is not quite so careful as the hybrid; for it might give you back a couple of collars and the other person a couple of shirts. The hybrid seldom makes a mistake of this sort. It has enough "sense" to know that two collars and no shirt are about as useless as two shirts and no collar for a complete outfit. The

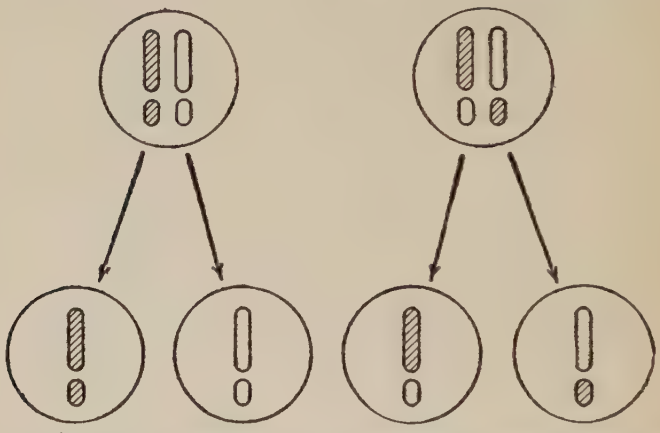

FIG. 21. Graphic representation of the reduction division to show two possible ways for the chromosomes to line up when there are two pairs.

hybrid would see to it that you get *a* collar and *a* shirt, one member of each pair of articles, so to speak, though it would not worry about which member of each pair you got. To get back to chromosomes, one member of each pair goes to every reproductive cell of a hybrid, but it is a matter of chance which member it happens to be (see Fig. 21).

In short, the segregation of one pair of chromosomes is *independent* of the other pair. This independence of segregation applies because one pair is not tied to the other, but the two are entirely independent of each

other. Each pair simply minds its own business, so to speak, and that is that both members of the same pair should not enter one of the reduced cells, leaving the other without any. The result then, is that the hybrids form four types of reproductive cells: *VP*, *vp*, *Vp*, *vP* (see Fig. 20 again). And these are formed in approximately equal numbers, because the segregation of the pairs is independent.

We have, however, not yet seen what the offspring of the hybrids are like; all we have so far is the composition of their reproductive cells. So let the hybrids mate and produce offspring. When they mate, their reproductive cells come together and produce fertilized eggs. But the sperm cells are a mixture of 4 different kinds of reproductive cells and so are the egg cells; and it is a mere matter of chance which kind will meet which in fertilization. For example a sperm cell containing the units *VP* might fertilize an egg cell containing the units *vp*, and produce a fertilized egg of composition $\frac{V}{v}\frac{P}{p}$ (where the units coming from the male are put above the lines, those coming from the female, below). This fertilized egg would develop into a fly that had long wings and red eyes. It would have long wings (not-vestigial) because not-vestigial (*V*) is dominant to vestigial (*v*). Its eyes would be red (not-pink) because "not-pink" (*P*) is dominant to pink (*p*). Take another possible combination at random. A sperm cell containing the units *vp* might fertilize an egg containing the units *vP*, producing a fertilized egg of composition $\frac{v}{v}\frac{p}{P}$. This would develop into a fly that had short

wings and red eyes (not-pink) because it is pure for *v*, the vestigial unit, that makes it short winged; and it has the dominant "not-pink" unit (*P*) that makes it red-eyed.

The two combinations just mentioned are by no means all that are possible. Let us go about matters systematically and see just what the possible combinations are. Suppose for the sake of simplicity that the sperm cells were all of one kind, let us say *VP*. Then they would fertilize any one of the 4 egg cells (*VP*, *Vp*, *vP*, *vp*), giving 4 types of fertilized eggs $\frac{V}{V}\frac{P}{P}$, $\frac{V}{V}\frac{p}{P}$, $\frac{v}{V}\frac{P}{P}$, $\frac{v}{V}\frac{p}{P}$ (where the units from the father are placed below the lines, those from the mother above). But there are 4 types of sperm cells in all, namely *VP*, *Vp*, *vP* and *vp;* and it is possible for any one of these types to fertilize all four types of egg, giving in all 16 possible combinations (see Fig. 22). These now grow up into the offspring, and the traits that they develop are determined by the units that they contain.

Not all of the combinations contain different kinds of units. Thus $\frac{V}{v}\frac{P}{p}$ has the same kinds of units as $\frac{V}{v}\frac{p}{P}$; they both develop into the same type of offspring. There are also offspring with different combinations that will look alike. Thus, $\frac{V}{V}\frac{P}{P}$ will have long wings and red eyes, but so will $\frac{V}{v}\frac{P}{p}$, because both *V* and *P* are dominant, respectively to *v* and *p*. If you add up the offspring that develop long wings and red eyes, you will

find 9 in all. Three will develop long wings and pink eyes, 3 short wings and red eyes, and 1 short wings and pink eyes. That is, you get the 9 : 3 : 3 : 1 ratio that Mendel got with his peas.

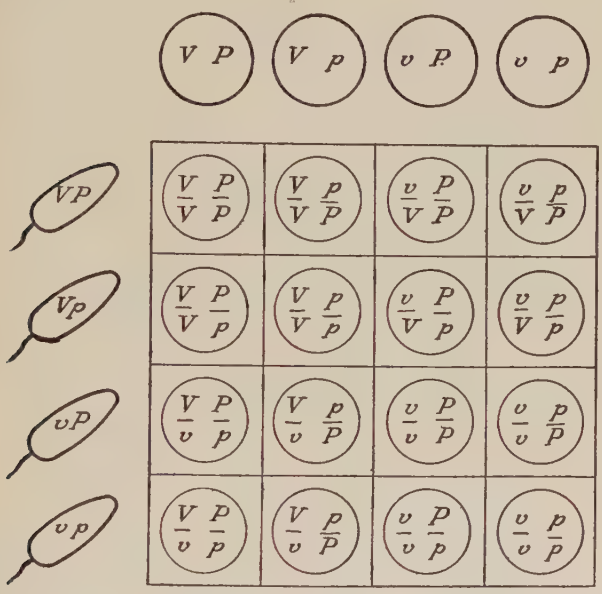

FIG. 22. Scheme to show how the reproductive cells combine in the cross $\frac{V}{v}\frac{P}{p} \times \frac{V}{v}\frac{P}{p}$.

The allelomorphs of the breeder are nothing more than the genes at a given locus. Allelomorphs run in pairs because the chromosomes do. They separate from each other and enter different reproductive cells because homologous chromosomes do this at the reduction division. Mendel found that one pair of allelomorphs segregated independently of another pair. This is also true of chromosomes.

Mendel made many crosses involving two pairs of allelomorphs. It so happened, in all his experiments, that he dealt with genes in different pairs of chromosomes. But one chromosome contains more than one gene, and had Mendel been dealing with genes in the same chromosome, he would have got a different result from the one he got. For a chromosome tends to be handed down entire to the offspring, and all genes that are in the same chromosome tend to be handed down to the offspring in a group and not as separate particles. They do not segregate independently of each other. But Mendel discovered a very important thing about genes when he found that allelomorphs did not mix with each other in the hybrid. This in fact, is fundamentally the Mendelian principle — the non-mixing of allelomorphs in the hybrid.

Mendel focussed his attention on what was happening in hybrids. He followed the allelomorphs. But animals and plants of pure type also contain allelomorphs, only in them both allelomorphs of a pair are the same, instead of different from each other. It would be theoretically conceivable that when two like allelomorphs came together, they mixed with each other, as might two paints of similar color, and that then the mass separated again into two equal portions. In this case the reproductive cells would be the same, so far as we could tell from the breeding results, as though no such mixture had occurred. In the hybrid, however, we are dealing with paints of different color, so to speak; and if they mix, the effect is apparent in the breeding results. But there is no such mixture in the hybrid and we assume that what applies to alle-

lomorphs in the hybrid also applies to allelomorphs in the pure type.

It should be borne in mind that any animal or plant may be hybrid at some of its loci and pure at others. It would indeed be strange if a different rule regarding segregation should apply to the various pairs of allelomorphs in one and the same cell at the time of the reduction division depending upon whether these allelomorphs were different from each other or alike.

As regards the exact nature of the genes, very little is known. There is, however, one very important thing that we do know about them in addition to the fact that they do not mix with each other. Every gene has the power of growth and every gene arises from a pre-existing gene through the process of growth and division. Genes never come into existence by the mere accumulation of their material independently of parent genes.

The lengthwise division of the chromosome into two, previous to cell division is the expression of the growth and division of its constituent genes. The new genes are exactly like the parent genes from which they grew. The newly formed chromosomes are also duplicates, because their genes are.

Note now why the chromosomes divide lengthwise, rather than across their middle. They do so because the dividing genes are strung out in a single file along their length — in "linear" order. When a new cell is formed through the regular method of cell division it receives a sample, so to speak, of a gene at every locus in the parent cell. The linear order of the genes in the chromosomes is the only order that readily permits of the proper distribution of the genes to a new cell. In

very rare instances, a cell does not divide by the regular method (mitosis), but constricts directly into two, nucleus and all, without first waiting for the accurate division and distribution of genes and chromosomes. Cells that are formed in this way (by amitosis as it is called) soon die, either they themselves or their descendants.

It is because the chromosomes have the power of growth and division that they can multiply as the embryo develops and that they can pass from the fertilized egg to all the cells of the adult. And it is further because the chromosomes segregate at the reduction division that different types of reproductive cells are formed in hybrids and that different types of offspring are produced, in definite ratios, through the union of the reproductive cells when the hybrids mate. The chromosomes in short afford us with the mechanism of Mendelian inheritance.

CHAPTER V

THE HEREDITARY BASIS OF SEX

Attempts of all sorts have been made artificially to cause an unborn child to be a male or a female at will. Especially have feeding experiments been tried on the mother before the birth of the child. But all such attempts have failed. One reason for their failure is that they were begun too late in development. In many instances the sex of the embryo was established long before the experiments were begun. In fact, a person is potentially a male or a female at the moment he begins his existence, and so all attempts at determining his sex after this very earliest stage of development have been futile.

The difference between the sexes extends right down to the details of their microscopic anatomy, to the cells that make up their muscles, nerves, skin and other parts of their bodies. The difference in their cells is not immediately apparent. In fact, you might carefully compare the skin cells of a male and female under the microscope and you probably would see no difference between them. But every cell contains a spherical body, the nucleus, and it is known on indirect grounds that the nuclei of the male and the female are not exactly alike. For the nuclei contain chromosomes, the rod-shaped bodies that carry our inheritance; and it is in the chromosomes that there is a difference. These bodies do not by any means differ so radically in male

and female. On the contrary, they are alike for the most part. In both the male and the female, there is a very peculiar thing about the chromosomes: as a rule they run in pairs (see Fig. 23). Pick out two chromosomes, a large and a small one, and you will find in the same cell another large and another small chromosome, the mates of the first two.

This rule regarding the pairing of the chromosomes applies without exception to the female. She has 48

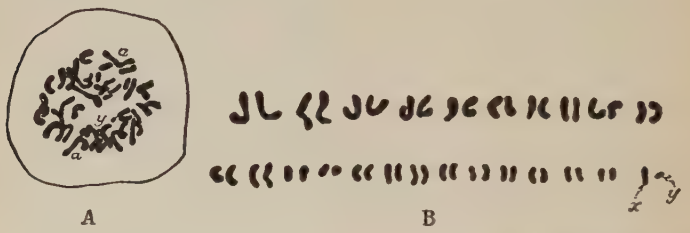

FIG. 23. The chromosomes of man, male. In *A* the chromosomes are shown as they occur in the cell; in *B* the "mates" are shown, as carefully singled out under the microscope from the cell shown in *A*. Note that all of the chromosomes form exact pairs (as "*a*" and "*a*") except the "*x*" and "*y*," the sex chromosomes. (Figure from Painter.)

chromosomes. These form 24 pairs. No one chromosome is left without a partner. But in the male, there is an exception to the rule. Most of his chromosomes run in pairs and you could match up all of them — except two. One of these is known as the *X*-chromosome; the other one is known as the *Y*-chromosome (see Fig. 23). In the female there is a pair of *X*-chromosomes, instead of an *X*-*Y* pair. This, in fact, is the only difference between the sexes, so far as chromosomes are concerned. But it is a difference that can be traced all the way back to the very earliest stage of development — to the time when a person is a fertilized egg.

It is just because the sexes are different at this very early stage that they are also different later, when their bodies consist of billions of cells. For the fertilized egg gives rise to all the later cells of the body — through the process of cell division — and in so doing, it hands down its chromosomes to them. It does this in a very definite manner for the most part. When it starts to divide to form two cells, it waits until all of its chromosomes have divided and formed two duplicate sets and then it hands down one set to each cell. The fertilized egg now has transformed itself into two daughter cells, both identical with itself in regard to all chromosomes, sex chromosomes included. A fertilized egg with two *X's* produces daughter cells with two *X's;* one with an *X-Y* pair produces daughter cells with *X-Y's*. The process of cell division is repeated over and over again. So long as the cells stick to the method of division just described, they continue to make duplicates of themselves. This they do in fact in most parts of the developing embryo. And so it comes about that practically all the cells of the adult body — billions in number — are either male or female in their chromosomal make-up. The fertilized egg has impressed its character upon them.

But how does the fertilized egg come to be either male or female? To see this, we must go to the reproductive cells that produce the fertilized egg. These cells are different from the ordinary cells of the body proper. They arise through a special type of cell division that takes place only in the reproductive organs of the male and female. In the female the two *X*-chromosomes come together, then separate and enter different cells

(see Fig. 24). In the male, the *X*-*Y* pair come together and then separate. The *X* enters one of the cells formed by the division, the *Y* enters the other one.

Note now that the eggs all have an *X*-chromosome. The sperm cells on the other hand, are of two kinds: half contain an *X*, the other half a *Y*. When fertiliza-

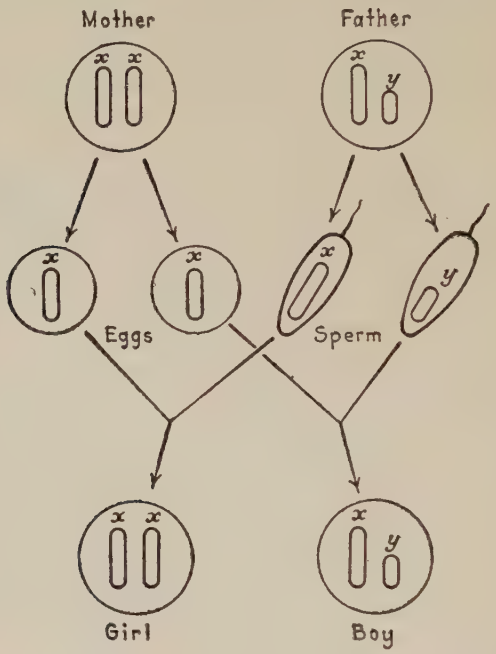

Fig. 24. Sex determination.

tion takes place, there are accordingly two possibilities. An *X*-containing sperm cell may fertilize an egg. This gives a female. On the other hand, a *Y*-containing sperm cell may fertilize an egg and this gives a male.

The general scheme of sex determination is very simple, but it sheds light on several things that were previously unexplained. Take the relative abundance

of the two sexes. In any country the number of boys and girls born is about equal, regardless of what food the people eat or under what peculiar conditions of life they may live. This fact in itself is rather surprising; and so long as we knew nothing about chromosomes, it was difficult to explain. But see how the chromosome mechanism clears things up. Half of the sperm cells contain an *X*, half contain a *Y*, and so the fertilizations that produce girls and boys are about equal.

In a family of six children or so, it does sometimes happen that all of them are either boys or girls. But here we are dealing with small numbers and it is entirely possible that there might be a run of one sex or the other just as a mere matter of chance. Toss up a coin six times and it may come heads or tails all six times. But toss it up a hundred times and you get the 50-50 ratio that you expect, or something close to it, as a rule. Just so with the sex ratio. When large numbers are involved, runs are less likely to cause a departure from the expected equality in numbers.

It is true, however, that even in large populations there is a slight departure from the expected equality in the sex ratio. Male births are somewhat in excess of female, about 103 of the one to 100 of the other. Though this difference is not so very large, it is more than would be expected on chance. Both types of sperm cells, the *X* and the *Y*-containing, are produced in equal numbers; and unless there is some source of disturbance, the fertilizations that produce the two sexes should be almost exactly equal in a large population. It has been suggested that the *Y*-containing

sperm — those that produce the males — possibly can move a little faster than their competitors and so reach the egg a little more often at the time of fertilization. The *Y*-chromosome is smaller than the *X*. Perhaps it lessens the load of the sperm cell a little and makes slightly faster movements possible.

It is often claimed that wars cause an increase in the proportion of male births. But how any such influence could operate is difficult to see. In some uncivilized communities female children are undesired and are disposed of either outright or through neglect, especially after a war, when males are at a premium. Even in civilized countries newly born boys might conceivably receive better attention in some cases than girls might after a war. In this event, the infant mortality among the boys would be relatively low and boys would come through in greater numbers than the girls. Unless we were careful not to confuse children born and living with total births, it might very well appear as though war caused an excess of male births.

It has also been claimed that the time at which conception takes place in the menstrual cycle of the mother determines the sex of the child, or that the thoughts and habits of the mother have something to do with the matter. It has even been stated that the egg develops into one sex or the other depending upon whether it comes from the left or the right ovary. There are many stories of this sort afloat. Most of them are in the nature of old wives' tales. Few or none of them have any substantial evidence to back them up.

Every now and then we hear an account of some animal breeder who claims he has found some method

of influencing the sex ratio. Undoubtedly he has tried something and found that it works apparently, but before we can accept his method as really effective we must be sure that he has found it to work in a large number of cases. Otherwise he might just be dealing with a run of one sex or the other, a thing which might very easily happen as a matter of chance in a small experiment. People also are apt to accept heresay evidence on sex control. No well confirmed method is really known for experimentally influencing the sex ratio in higher animals.

Our knowledge of the sex chromosome has helped us to understand the difficulties in the way of artificially determining sex. It has also shed light on another matter. Women are much less often color blind than men. What is more, if a woman does happen to be color blind, all of her sons are also color blind, but none of her daughters are as a rule. A color blind man, on the other hand, seldom has any color blind children, either sons or daughters; but some of his grandsons might be color blind, and they practically always are the offspring of his daughters, not of his sons.

We can readily understand all of this on a simple assumption. The hereditary basis for color blindness is to be found in the sex chromosome. A color blind woman carries an hereditary unit, — a gene — for color blindness (*c*). This she carries in both of her *X*-chromosomes (see Fig. 25). A normal man carries in his *X*-chromosome the normal gene (*C*) instead of the color blind gene. His *Y*-chromosome we may regard for the present as an empty sack that carries no genes.

Consider now how the sex chromosomes and their

units are transmitted to the children of two such persons (see Fig. 25 again). The color blind woman produces eggs all of which contain an *X*-chromosome, including the color blind gene (*c*). The normal man

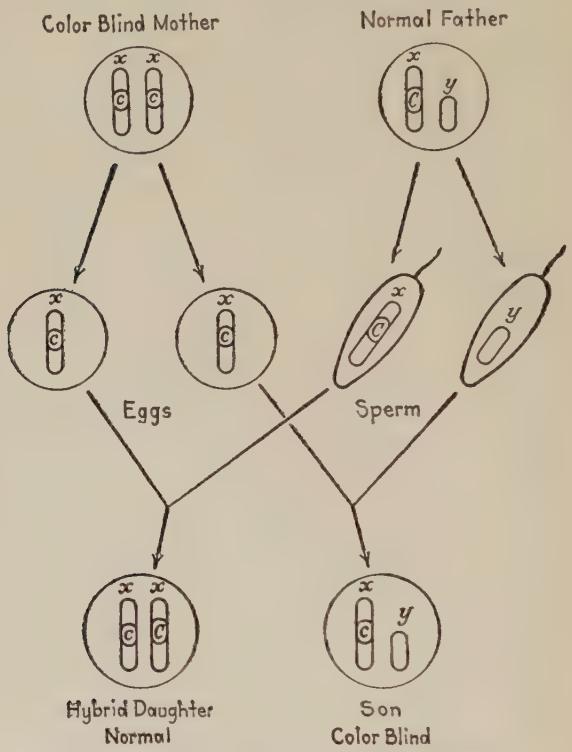

Fig. 25. Inheritance of the color blind gene.

produces sperm cells of two types, half with the *X*-chromosome and its normal gene (*C*), the other half with the *Y*-chromosome. When fertilization occurs, there are two possible combinations of reproductive cells. An egg cell may be fertilized by a sperm cell that contains an *X*. It might also be fertilized by one that contains a *Y*.

The first combination produces a daughter who has both *C* and *c* (see Fig. 25). But she develops into an apparently normal person, because *C*, the normal gene, is dominant to *c*, the color blind gene. The second combination of reproductive cells (an egg cell fertilized by the *Y*-containing sperm) produces a son. He has *c* in his *X*-chromosome. He has nothing in his *Y*-chromosome. This leaves him with the color blind gene alone, and he develops color blindness.

Consider now the other mating — a normal woman with a color blind man. A normal woman might conceivably be a hybrid and carry both *C* and *c*, as do the daughters in the first mating. But if there is no color blindness in her family she would not carry the color blind gene. She would have the normal gene (*C*) in each of her sex chromosomes; and as a rule this would be the case because most normal women in the population at large are pure normals rather than hybrids. We may then regard the woman in the mating under discussion as free from the color blind gene. Her husband, however, is color blind and carries the gene in his sex chromosome.

Consider now how he and his wife transmit their genes to the children (see Fig. 26.) The mother produces eggs each with a normal gene. The father produces sperm cells, half containing the *X*-chromosome with its color blind gene, the other half containing the *Y*-chromosome. In fertilization, the *X*-*X* combination produces the daughters. They have both *C* and *c*. The *X*-*Y* combination produces the sons. They have only *C*, the normal gene, and are not color blind. Neither will they have color blind children, provided

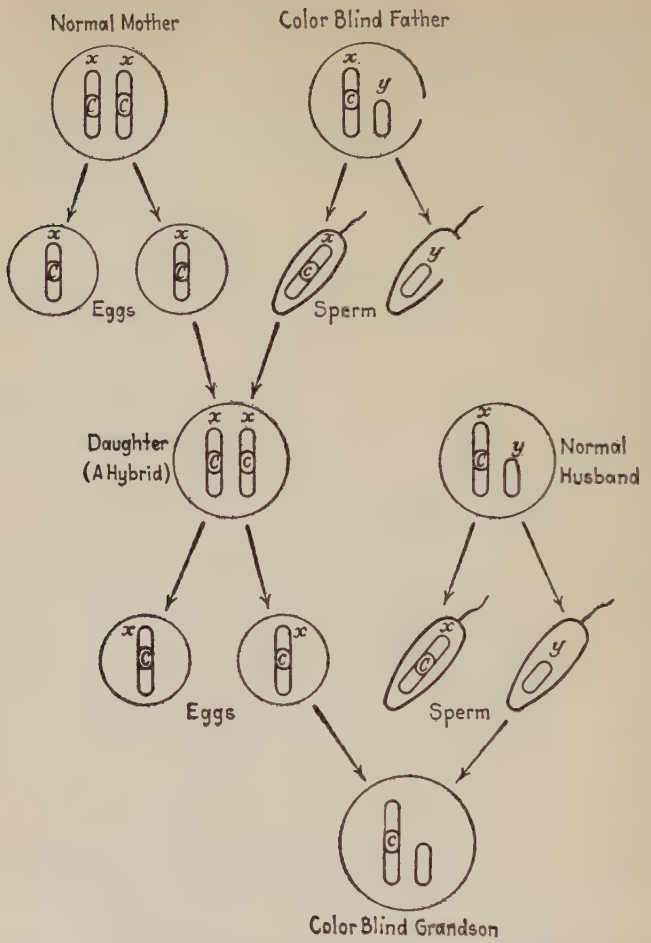

FIG. 26. Transmission of color blind gene from father to grandson, through the daughter. Not all the possible combinations of reproductive cells are shown, but only those that show how the gene gets to the grandson.

they do not marry women who carry the color blind gene. But with the daughters it is different. They carry the color blind gene and can transmit it to their children (see Fig. 26 again). Any of the sons that

happen to receive it will develop color blindness. This will be the case regardless of whether or not their father is normal; for they receive from him his *Y*-chromosome, without any *C*. The daughters on the other hand will probably not develop color blindness, for all of them receive an *X*-chromosome from their father. If he is normal as he probably would be, he will transmit with his *X*-chromosome the normal gene; and his daughters will develop normal sight regardless of whether or not they receive the color blind gene from their mother.

Note now that a son has just one *X*-chromosome and that he receives this from his mother. If she is color blind, he too is bound to be. A daughter on the other hand has two *X*-chromosomes; one she receives from her mother, the other from her father. Unless both her parents carry the color blind gene, she herself cannot be color blind. Should she receive the normal gene from either of them then she would develop into a normal person.

It is apparent from this why color blindness is much scarcer among women than men. For a marriage to produce color blind males, it is necessary that only one of the parents, the mother, carry the color blind gene. But if the marriage is to produce color blind females, both parents must carry the gene. Any such coincidence would be very unusual.

Genes for two other abnormalities besides color blindness are known to occur in the sex chromosomes, abnormalities known as "hemophilia" and "night blindness." Persons afflicted with hemophilia have a tendency to profuse bleeding from slight wounds because their blood fails to clot upon being shed. In

night blindness, unusual difficulty is experienced in recognizing objects at dawn or dusk, or whenever the light is not of full intensity. Both defects are recessive to the normal condition.

Much of our knowledge of the sex chromosome was made possible by studying first the lower forms of life. Insects gave us much valuable information. It was discovered how sex was determined in them long before the facts were known for man. But then biologists reasoned that the same principle of sex determination should apply to man and they began to look for the sex chromosome in him. A special technique is necessary in searching for the chromosomes. A small piece of fresh tissue from some part of the body is got and after it is properly hardened by chemicals it is sectioned very much in the way that meat is sliced by a meat-slicing machine. The instrument used for the purpose is very sharp and accurate, and is capable of cutting slices less than a thousandth of an inch in thickness, slices so thin that the cells are seen in a single layer when they are examined under the microscope. The sections are also treated with special stains that bring out the chromosomes. The best tissue in which to see chromosomes as a rule is the testis of an animal. In the case of man, it was necessary to get the testes from recently executed criminals or from persons who were castrated on some medical ground. The tissue had to be fresh; it could not come from a person who had been long dead; otherwise the chromosomes would clump up and be difficult to study in minute detail. It was not easy to get fresh material in the necessary amount for repeated and careful examination in the case of man, and

unless lower animals had already paved the way and given biologists an idea of what to look for, it would have been almost impossible to discover the sex chromosomes in man.

The study of lower animals too made it possible to understand such a case as color blindness in man. The way again was paved by an insect, Drosophila. Biologists[1] kept this animal under close observation in the laboratory and noticed the sudden appearance every now and then of a fly that was peculiar in some way—a "mutant." One of the "mutants" that they observed had white eyes instead of red. They now crossed a white-eyed female to a red-eyed male and found that all the sons from the cross had white eyes, all the daughters had red eyes. The case is obviously like color blindness in man.

In working with Drosophila, it was observed that occasionally half the sons in a family were missing. The number of offspring in a Drosophila family may be very large, three or four hundred. When some families were found with only half as many sons as daughters, it was safe to conclude that half the sons had failed to develop. This case does not at first sight look like the color blind case in man, but it really has the same explanation. Consider again a mother who is hybrid for color blindness $\left(\frac{C}{c}\right)$. Half of her sons are normal, half are color blind, according to whether they receive the sex chromosome with C, or the one with c. Suppose now that c caused some weakness that was really serious, and not merely color blindness; a weakness that was

[1] A group of men working at Columbia University.

fatal to the developing embryo. Then the sons who had *c* would never reach maturity, and so half of the males in the family would be missing. This is precisely what happened in the Drosophila families under discussion. The mothers contained a gene that killed half the sons, or at least prevented them somehow from developing. Let us call a gene of this character a "lethal," and designate it by the letter *l*. The mothers themselves

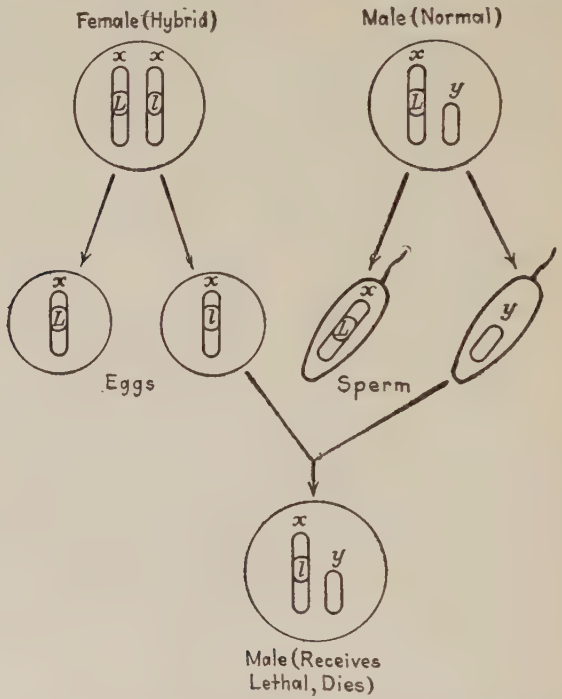

FIG. 27. Transmission of lethal gene from the female parent to a male offspring. Not all the possible combinations of reproductive cells are shown.

were not killed by the lethal gene. They were hybrid and contained the normal allelomorph (*L*) that was dominant to the lethal (*l*) and that prevented the lethal

from expressing itself. The mother in terms of symbols was $\frac{L}{l}$. The half of her sons that got the normal gene (L) developed. But the other half that received the lethal (l) failed to develop and were missing when the off-

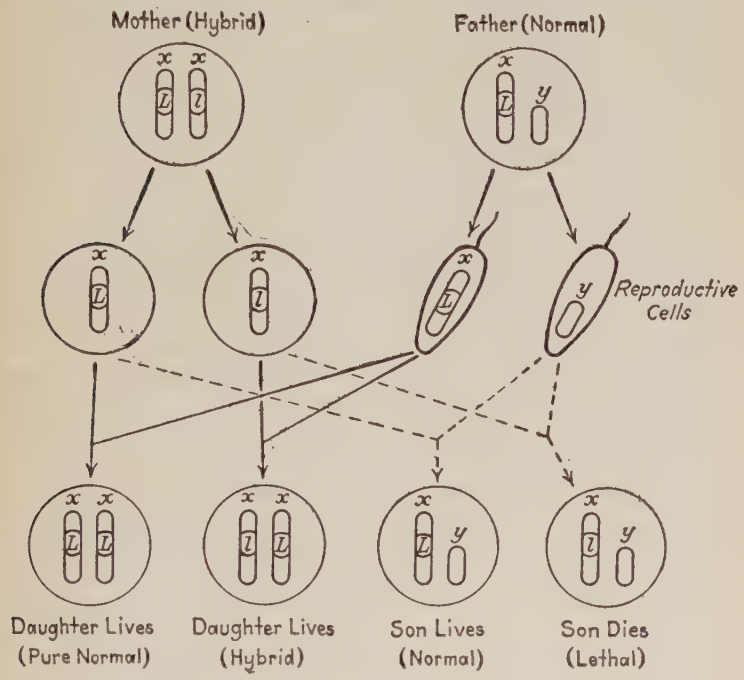

FIG. 28. Transmission of a lethal gene — complete scheme.

spring were counted (see Fig. 27). None of the daughters in the family were missing. Half of them, it is true, received l from their mother (see Fig. 28), but they also received a sex chromosome from their father, and got the normal allelomorph (L). They were hybrids $\left(\frac{L}{l}\right)$ like their mother. Accordingly, the count of the

offspring in the family gave the peculiar sex ratio of 2 females to 1 male, instead of the ordinary 1 to 1 ratio (see Fig. 28 again).

From the studies made on Drosophila it became evident that the entire *X*-chromosome was not concerned with the determination of sex. A certain portion of the chromosome is occupied by genes that have nothing to do with sex. But these are tied up in inheritance with the part that has to do with sex itself and accordingly are said to be "sex-linked." Just how much of the *X*-chromosome is concerned with sex itself, is not known. Whatever the amount may be, it normally produces maleness in one "dose," so to speak, femaleness in two, in accordance with whether the cell has one or two *X*-chromosomes.

The *Y*-chromosome does not seem to have very much to do with sex development, though it is the partner of the *X* in the male. This fact is indicated by studies made on lower animals. One of the species (the fruit fly) which normally contains a *Y*-chromosome has been found occasionally to produce males that develop without the *Y*-chromosome. The male, apparently, does not need the *Y*-chromosome for his development.[1] Moreover, in some species there is no *Y*-chromosome normally present in the male. It is possible, in fact, to arrange a number of species in a series, beginning with those that have a *Y*-chromosome as large, or almost as large as the *X*, down through intermediate steps to those that have no *Y* at all. In all these cases, however, the male has an *X*.

The difference between the sexes in lower animals is

[1] But in Drosophila males lacking a *Y*-chromosome are sterile.

not always a matter of one or two *X*'s as in man. Birds and butterflies conform to a somewhat different scheme. In them, the male has a pair of chromosomes that have been labelled *Z-Z*. The female has a pair that are not exact mates, *W-Z*. The *W* somewhat resembles the *Y* of man in that it seems to have no important influence on development. The *Z*, however, is different from the *X* of man in its action on sex. One dose of the *Z* produces a female, two a male. Just the reverse is true of the *X*. It is rather odd that there should be two different formulas for sex determination in the animal kingdom. But the two have a point in common. In both, sex determination is a matter of chromosomes, and in both a certain chromosome throws the developmental balance in favor of one sex or the other, depending upon whether the cell contains one or two doses of the chromosome in question.

A very curious and exceptional case of sex determination has been found in bees. It is bound up with a peculiarity in the way bees sometimes reproduce. The eggs of these animals may develop into normal adults without fertilization, a process that is known as "parthenogenesis." All eggs of the bee do not develop without fertilization. The queen bee carries a store of sperm cells in a pouch connected with her oviduct. These she received from a male at the time of copulation. When she lays an egg, she sometimes fertilizes it, sometimes not. The eggs that she fertilizes develop into females. The unfertilized eggs develop into males. The females may become either queens or workers, depending upon the amount and kind of food that they receive during their development. The males are the drones.

Notice now that the two sexes have a different number of chromosomes in bees. The male is produced without a sperm cell and so lacks the set of chromosomes that usually come from the male parent. The female on the other hand receives chromosomes from both sperm and egg cells in the usual way for animals and so has the double set of chromosomes. The actual number in the male is 12; in the female, 24. These are the numbers in the fertilized eggs from which male and female develop. They are also the numbers in all cells that are derived from the fertilized eggs in the ordinary manner. But the reproductive cells of most animals contain half the number of chromosomes found in the ordinary cells, due to a certain type of cell division (the "reduction" division), that brings about a reduction in the number. This takes place in the female bee as usual, giving us half of 24 or 12 chromosomes in every egg. But the ordinary cells of the male already contain the reduced number of chromosomes (12). Accordingly a reduction division is unnecessary in the male and is omitted.

Up to this point, we have been dealing with animals that are either male or female; but many plants and a fairly large number of animals known as hermaphrodites have the two sexes combined in the same individual. Earthworms are both male and female; so are snails and many other slow moving animals. It might seem offhand that chromosomes should explain the hermaphrodite, but there is no evidence that the female part of an hermaphrodite is any different, in its chromosomal make-up, from the male part. The reason why one part of the animal develops ovaries and another

part testis, is not really a problem of inheritance, but one of development.

The reproductive organs of the hermaphrodite present a problem that is very much the same as for other organs of the body. One part of an animal can develop eyes, another part ears. Yet the cells in any two such parts of the animal's body are not, so far as we know, any different in their chromosomal make-up. The animal's cells simply have the power to develop into either eyes or ears, depending upon where they happen to be located in the developing cell mass. Just so with the reproductive organs of an hermaphrodite. The conditions in two parts of a developing animal are not the same, and in an hermaphrodite these differences may be sufficient to determine that one part should develop ovaries, the other testes. In animals with separate sexes the problem is somewhat different. Two individuals develop in the uterus of the same mother and under exactly the same conditions. Yet one may become a male and the other a female. The difference between the two in this case is a matter of heredity and is dependent upon chromosomes, not upon environment.

Studies made on a certain snail-like animal (known as Crepidula) indicate that chemical substances may have an effect on sex in an hermaphrodite. In this particular hermaphrodite, the male organs as a rule appear before the female and also disappear before them, so that an individual is a male when young, then an hermaphrodite, and finally a female when fully grown. The young animal, as a rule, attaches itself to a female, develops the male organs, and remains small for some

time, as long as the female is fertile. It then grows to the adult size and becomes a female. Another young animal attaches itself to the newly developed female and enters upon the male stage of development. If, however, the young animal does not come into contact with a female, or near one, it skips the male stage and grows rather rapidly into a female. It seems likely that the female gives off some chemical substance that causes the young animal to develop the male reproductive organs.

External conditions rather that the chromosome mechanism may in rare instances determine sex even in the case of animals with separate sexes. There is a curious case of this sort in a lower animal. A certain species of worm, known as Bonellia, consists of large females, but very small males, less than a quarter of an inch long, which live on the proboscis of the females. When the animal is very young it may do one of two things. It may find its way to the proboscis of a fully developed female, in which case it develops no further and becomes a diminutive male; or it may be independent and grow to a full sized individual, a female. Here apparently, the environment determines whether an egg shall develop into a male or into a female.

A peculiar case has been reported in chickens. It has been claimed [1] that a female gradually changed over to a male. The animal had tuberculosis. Its ovary disappeared and was replaced, according to the report, by testes. This report further states that early in its life the animal layed eggs and had the plumage and typical appearance of a hen. Later it developed male plumage and functioned as a rooster.

[1] By F. A. E. Crew, of The University of Edinburgh.

In man there occur very rarely individuals, referred to as hermaphrodites, who have the reproductive organs of both the male and the female partially developed. They are not hermaphrodites in the sense that they have both ovaries and testes of the normal kind. Their external reproductive organs are partially male and partially female, but are very poorly developed and not capable of functioning either as those of a male or a female. Some hermaphrodites are more inclined towards the male type than the female, others more towards the female. It seems probable that in a good many instances hermaphrodites started life from the fertilized egg with the chromosomes typical of one sex or the other, but that some disturbance set in that influenced their reproductive organs, a disturbance possibly in the form of chemical agents from some gland in the mother or from some deranged gland in the embryo itself.

An explanation of this sort is suggested by an observation in lower animals. In cattle, there are born occasionally abnormal calves known as "free-martins." These animals are females externally but their internal reproductive organs and the ducts leading to them are poorly developed, and they may even be inclined towards the male type. Curiously enough, a free-martin is always one of twins. Not only this, but the other twin is always a male; and it is the male that has caused the female to develop abnormally.

The male does not always have this influence on a female that is developing in the same uterus. It takes place only when there is established a connection between the circulation of the two embryos

through the fusion of the membranes (the chorions) that surround each embryo. Ordinarily, the blood passes by way of the umbilical cord from the embryo to the membranes and then back again to the embryo. But when the two membranes are joined, the blood can circulate from one embryo to the other; and it is in the blood stream that there is carried a chemical agent (a hormone), secreted by the testes of the developing male, that favors the development of the male reproductive organs and acts as a check on those of the female.

Just what causes hermaphrodite tissue in man is not definitely known. A derangement in a certain gland connected with the base of the brain (the pituitary gland) is sometimes accompained by defective development of bodily form. In a male so affected the hips are abnormally broad, the shoulders narrow and the breasts prominent. But the reproductive organs are male, not hermaphroditic. It is conceivable that a derangement of some gland might influence them too and cause hermaphroditism.

Whatever the explanation may be of human hermaphrodites, it seems reasonable to assume that they began life with the chromosomal make-up of males or females, and under normal conditions of development would have grown into normal males or females; but that other influences set in and interfered with the normal course of events.

Among the insects there are sometimes found individuals known as "gynandromorphs" that are male in one half of their bodies, female in the other half. The difference between the two halves of the body in-

volves not only the reproductive organs proper, but also other parts. In the fruit fly, for example, the female has a larger body than the male, and in an animal that is half male and half female, the body is twisted to one side on account of the size difference of the two halves. Also, the male half of the body is black at the hind end, the female half is not. There are other differences as well.

A gynandromorph in the fruit fly begins life as a female. There are two *X*-chromosomes in the fertilized egg from which it develops. In normal cases of development the fertilized egg divides to form two cells, each with a pair of *X*-chromosomes. But in an animal that becomes male in one half of its body, an *X*-chromosome belonging to one of the cells gets lost during the course of the first cell division, and the cell that lacks this chromosome has now only one *X*-chromosome and develops into the male half of the body (see Fig. 29). The irregular cell division may occur late in life, rather than at the first cell division. In this event, half of the body would not be formed from it, but only a small patch of cells; and then only this patch would have the characteristics of the male. If the irregular division occurred at some intermediate period the part of the body that was male would be of intermediate amount.

In man and the higher animals, the removal of the ovaries or testes in the young individual interferes with the normal development of other parts of the body, such as the voice and beard in the male and the breasts in the female, parts that are referred to as secondary sexual characters. Their development is dependent upon chemical agents, known as hormones, that are

secreted by the reproductive organs. But the chromosomes normally determine whether an animal is to have ovaries or testes and so ultimately determine the secondary sexual characters.

If sex is ever to be controlled in man, it will probably have to be done through the chromosome mechanism. It will be the father who will have to be experimented

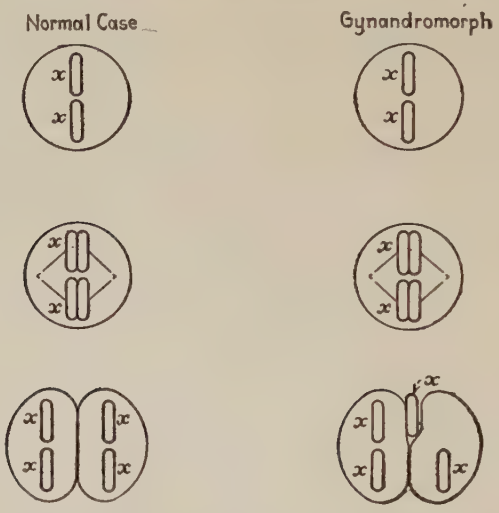

Fig. 29. Diagram to illustrate the theory of the gynandromorph.

on, rather than the mother, for his sperm cells determine whether the child is to be a male or a female. Possibly some drug might be found that could injure one type of sperm or slow up its movements, leaving the other to fertilize the egg and produce a girl or a boy, according to whether the sperm cells were of the female or male determining type. It is conceivable that a hormone or drug might be found that could influence the sex development of the early embryo, regardless of

its chromosomes, or even reverse its sex development, as suggested by the case in chickens. But probably human beings whose sex development had been determined in this way would not be fully normal, and it would be better to attempt the control of sex through the normal mechanism, the chromosomes.

It seems not so very unlikely that we shall be able to control sex some day, possibly in the near future. If so, there might be an excess of boys or of girls born, according to the sex that happens to be in vogue. The scarcer sex would then automatically come into greater favor and in the following generation would tend to be produced in excess. In this way, it is conceivable that sex control may raise difficult sociological problems which will have to be faced and solved.

CHAPTER VI

HOW THE RACE EVOLVES — MUTATION

It has often been stated that if some external influence acted on a race generation after generation, its effect on the race would become so deeply ingrained as to be eventually inheritable. So, for example, the black race is sometimes supposed to owe its origin to the tanning effect of the tropical sun, one generation handing down its darkened skin to the next. According to this view, a man can transmit a tanned skin to his offspring.

Most students of heredity do not hold to any such view. The evidence at their disposal indicates that the sun does not affect the skin of the unborn child; that he is just as light as if his parents had never been darkened by the sun.

It is true that dark races tend to evolve in the tropics and that the sun has something to do with the process. But it does not follow by any means that tanning is inherited. The origin of the dark race probably has a totally different explanation. According to the modern genetic view, parents who are pure white by birth have offspring who are almost without exception also pure white, regardless of how much their parents were tanned. But occasionally there is born of pure white parents a brunette child. His darker skin had nothing to do with the sunlight. He was simply born that way, for no known reason. He is a freak in the sense that

he is different from the vast majority of other children having similar parentage. He is technically known as a *mutant*, and the change that produced him, a *mutation*. From him a darker skinned race might arise; for some change has occurred in his hereditary make-up, and he is able to transmit the change to his offspring.

Probably no more brunette mutations take place in the tropics than in the north. That is to say if a group of pure white people should migrate to the tropics and get tanned they would not produce any greater percentage of brunettes than if they lived in the north and were untanned. But in the tropics, the brunette children would have an advantage over the pure white, because a dark skin protects them against sunstroke. The brunettes stand a greater chance of reaching maturity and leaving offspring than their less fortunate fellows. In this way, they would gradually displace the lighter-skinned type. Further mutations would occur which would make the brunettes still darker. They in turn would displace the lighter brunettes, and so the race would eventually become very dark. The whole process would probably require thousands of years for its completion; first, because mutations are very infrequent, and second because the new types that arise by mutation would not immediately displace the old, but only in the long run.

The tropical sun plays a part in the evolution of the darker race, but not a direct part. It does not cause the mutants to appear. All that it does is to favor them after they have made their appearance. It weeds out the lighter types and makes more room for the darker. In brief, it is merely a *selective agent*.

This account is totally different from the one which claims that the sun directly causes the evolution of the darker race. The older view would be correct only if tanning were inherited. But there is no evidence whatever to support such a view. When a person is born with a skin darker than usual there is something in his hereditary make-up which is different from that of the ordinary person's and which makes it possible for him to develop his darker skin entirely apart from the tanning influence of the sun. The trait has an hereditary basis. A tanned skin, on the other hand, is an acquired trait in the sense that it has no special hereditary basis. It is dependent for its production upon some outside influence, the sun. If tanning were really inherited it would be an example of what is known as "the inheritance of acquired characteristics," a thing for which we have no evidence.

There are various facts which superficially suggest an inheritance of acquired characters and which have been offered in support of the view. None of the facts in question really do support the view; they all have the same explanation as has the origin of a dark skinned race. Take the case of fish and lizards that live in dark caves, and that have lost their eyes in the course of evolution. It might seem offhand as though these animals were blind because the darkness had weakened the eyes of their ancestors through disuse and that the weakened condition so produced was handed down from generation to generation until the race had finally become blind. We are not necessarily driven to such an explanation. It is quite possible that the loss of eyes came about through mutations. In a dark cave eyes are

of no value; in fact they are a handicap because they are subject to continual injury. Any mutations that led to partial or complete loss of the eyes would therefore be of advantage. The animals that had the mutations would have an advantage over the ordinary animals with eyes and would eventually displace them. Darkness merely favors the eyeless mutants in the competitive world and helps them to spread. It again is a selective agent just as was the sunlight in the evolution of a dark skinned race. But what causes the appearance of the mutants in the first instance is not known.

The "degeneration" of parasites has an explanation similar to the one just given for the loss of eyes in cave-dwelling animals. The loss of organs that are not used by the parasite is not due to an inheritance of the effects of disuse. Any organs which a species does not use are merely a hindrance to it and the species is better off without them. Mutations that lead to their loss will therefore be preserved and the species will "degenerate," or to use a better term, it will become "simplified."

The various facts which supposedly suggest an inheritance of acquired characters all have a certain point in common. Take the case of tanning. It so happens that the race may acquire through mutation a trait (dark skin) which resembles one that the individual acquires as the result of an environmental influence (the sun). That is to say the individual acquires certain traits in direct response to certain conditions in the environment and the race may acquire similar traits but through mutation. It does not follow at all that the acquired trait and the mutant have the same

cause simply because the two appear the same. The particular environmental conditions that produce an acquired trait do not necessarily also produce a mutation of similar appearance. Sunlight does not cause mutations for darker skin simply because it causes tanning. But because sunlight acts as a selective agent in their favor after they have made their appearance, it may superficially seem to cause them to make their appearance.

It is entirely possible that light and other environmental agents cause mutations. But at present we do not know what kinds of mutations, if any, they bring about. The effect of an environmental agent, say the sun, on the parent is a totally different thing from its effect on the unborn offspring. In the one case it acts directly; in the other it can act only indirectly through the reproductive cells of the parent and through the complicated machinery of inheritance. It is impossible in the present state of our knowledge to predict what effect most agents have on heredity; least of all are we in a position to affirm that a given agent will produce a mutant of a certain kind on the ground that it produces a bodily change of a similar kind in the parent. In brief, there is positively no known relationship between bodily changes and mutations.

Whatever the cause of mutations may be, their actual occurrence is a fact. The evidence for them has been supplied by the lower forms of life, especially by a certain insect commonly known as the fruit fly (Drosophila). This animal has been kept under close observation in the laboratory for many years, during which time hundreds of generations were grown. Large num-

bers of flies, millions in fact were carefully examined, many of them under the microscope, and were observed to conform almost without exception to the normal type. But occasionally there was produced an offspring which was noticeably different from other members of the species. Sometimes the eyes were white instead of red, the body yellow or black instead of grey; sometimes the wings were missing or shorter than usual, etc. The mutants in question were not merely mutilations or cases of defective development. For if they had been their offspring would not have shown the change. The new trait was actually due to a change in the hereditary make-up of the species because it persisted. It arose through mutation. From it large numbers of descendants were got all having the new trait. In this way a new race had its origin.

During the period that Drosophila was kept under observation in the laboratory several hundred mutants made their appearance. To discover this number of mutants it was necessary to examine carefully millions, literally millions of flies. For it was only with extreme rareness that a mutation occurred. Moreover, when one did show up, there was no apparent reason for its occurrence. The particular fly in which the mutation was first noticed may have been just one of several hundred offspring all of which came of the same parents and grew up under the same conditions so far as could be observed. The flies were raised in milk bottles with banana as food. The conditions within a given bottle were probably pretty much the same for all the flies; still, just one fly in a bottle might be a mutant, and the rest all normal. The mutated fly may also

have had several thousand cousins grown in other bottles, all normal in every respect. Just why the mutation should have occurred in the one particular fly is not known.

It was found possible to cross the new races to each other and to combine in one fly the various mutations that had arisen separately. In this way one new type of fly was got that looked totally different from the normal race. It resembled an ant in outward appearance more than the fly. So different was it from the parental type that no student of insects would have hesitated a moment in considering it a species by itself on the basis of its outward appearance. Thus a new form of life had come into existence under the very eyes of the laboratory worker through the process of mutation.

The various new races were also crossed to the parent race in order to see what the offspring would be like. In the first generation the offspring as a rule all resembled the normal type. But when the first generation bred with each other and produced offspring of the second generation the new type reappeared, alongside with the old. The two types appeared in a definite ratio, three of the old to every one of the new, on the average. This is precisely the ratio which Mendel got when he crossed one race of peas to another.

It is now understood why mutants should behave in crosses like Mendel's races of peas. A mutation represents a change in the hereditary make-up of a species. When for example a wingless race (known as "vestigial") arose by mutation in Drosophila it was not primarily the wing that changed but something upon

which the development of the wing depended. To trace the mutation to its original source we must not look at the wing itself and the mere visible change that occurred in it but we must go to the microscopic units that make up the animals, the cells, and continue to go even farther, into the nucleus of the cells. Here it is that there are contained certain rod-shaped bodies, the chromosomes, that determine the character of the animal. For the chromosomes contain the units of inheritance, the genes, and it was in one of the genes that some change occurred which later expressed itself in the loss of the wings.

The change in the gene may have occurred long before it was actually noticed by its visible effect on the wing; in fact it may have taken place way back in one of the grandparents of the wingless animal, and in just one of the cells of this grandparent. But the cell in question was a reproductive cell, or one that gave rise to reproductive cells, and so it was possible for the changed gene to be handed down to the offspring. They themselves might not have shown in the first generation any evidence of the mutation. For they received not only the changed gene (call it "*v*") from the parent in which the change actually occurred, but also the normal gene (*V*) from their other parent. The first offspring to receive the changed gene were therefore hybrid $\left(\frac{v}{V}\right)$; and it so happens that the development of the hybrids is determined in this particular case by the normal, rather than the abnormal gene that they contain. For this reason, they had wings. But before the hybrids reproduced, they formed reproductive cells of two types,

one containing the normal gene (V) and the other the mutated gene (v). Now when the hybrids mated, it was possible for two reproductive cells to come together each with the mutated gene (v). There were formed as a result fertilized eggs that contained a couple of mutated genes $\left(\frac{v}{v}\right)$. These flies were of pure type rather than hybrid and in them the mutated gene could manifest itself and cause them to develop without wings. From matings of the pure type nothing but wingless offspring came and so the new race was fully on the way.

By mating the pure race $\left(\frac{v}{v}\right)$ with the parent race $\left(\frac{V}{V}\right)$ it was found possible to get hybrids $\left(\frac{v}{V}\right)$ at will and by inbreeding the hybrids offspring of two types were got, some of them winged, others wingless. The hybrids produce the two types of offspring because they have reproductive cells of two types, half containing the unmutated or normal gene V and half containing the mutated gene v. When two normal genes come together in fertilization $\left(\text{giving } \frac{V}{V}\right)$ or when a normal and a mutated gene come together $\left(\text{giving } \frac{V}{v}\right)$ a fertilized egg is formed from which normal offspring develop. It is only when two mutated genes come together $\left(\frac{v}{v}\right)$ that an offspring of the new type develops. The two types, old and new, appear on the average in the relative proportions of 3 : 1, and thus fall into the same ratio

that Mendel got in the second generation from his pea crosses.

It will now be apparent why the mutated gene is inherited in Mendelian fashion. In the old race there is a pair of genes $\left(\frac{V}{V}\right)$ that separate from each other before the animal forms its reproductive cells (giving V and V). In the hybrid $\left(\frac{v}{V}\right)$ one member of the pair (v) is different from the other (V) because it has mutated from V to v, but the new gene still continues to separate from the old one just as it did before it mutated. The process of mutation has not affected its "habit" so to speak, of separating from its mate and entering a different reproductive cell. To put the thing in technical terms, a gene continues to segregate from its allelomorph (its partner) after mutation, just as it did before. It is for this reason that the hybrid $\left(\frac{v}{V}\right)$ forms two types of reproductive cells, one with the normal gene V, the other with the mutated gene v. When hybrids mate, they produce two types of offspring, the old type and the new, corresponding to the two types of reproductive cells. The 3 : 1 ratio into which the offspring fall results merely from the chance combination of the reproductive cells.

Whenever a new kind of gene comes into existence it always does so by mutation from a pre-existing gene. It continues to separate (or segregate) from the old type when the two come together in a hybrid. The Mendelian ratio is nothing more than an expression of this fact and is in itself evidence for mutation.

Mendel did not know what was the origin of his races of peas, but it is probable from their behavior in crosses that they too arose by mutation just as did the different races of Drosophila. It is moreover probable that all new forms of life have arisen by mutation because all inheritance seems to be Mendelian.

In considering the wingless race of Drosophila note especially that the loss of the wings did not come first and then the hereditary change. But the thing is just the other way around: the change in the gene, the actual mutation came first and then the loss of the wings, the manifestation of the mutation. If there were an inheritance of acquired characteristics, then indeed the bodily change would come first and it would perpetuate itself in future generations by causing a hereditary change of the right sort. This would be an inversion of the true order of events.

Mutations are the only type of hereditary change that the biologist has been able to demonstrate in his laboratory. He has never been able to get indisputable evidence for an inheritance of acquired characteristics through well controlled experiments. One worker[1] tried cutting off the tails of the rats for a large number of generations but rats continued to be born with tails. His experiment was really unnecessary in view of the practice of circumcision continued over several thousand years by the Jews. Another worker[2] removed the ovaries of a white guinea pig and substituted for them those of a black guinea pig. His idea was to see

[1] Weismann, a German biologist of the latter part of the nineteenth century.

[2] Castle, of Harvard University.

whether the ovaries would change to the white type because of the white coat color of the animal to which they were transplanted. He waited until the guinea pig recovered from the effects of the operation, then mated it to a white male. If the ovaries of the female had really changed to the white type then the reproductive organs of both male and female would have been of the white type and the offspring should be white. But they were all of them black, even though some were born a year after the operation.

None of these experiments, it might be claimed, are really fair tests for they all involve surgical operations and never occur in nature. We have, however, much better evidence to which this objection does not apply and which indicates that acquired characters are not inherited. The evidence in question was derived from bean plants. Experiments were conducted[1] on the size of the seeds. Everybody knows that no two seeds on the same bean plant are of exactly the same size. They vary in accordance with the size of the pod from which they come as well as their position in the pod. In the experiments in question, some bean plants were grown from the smaller seeds, others from the larger seeds of the same parent plant and the size of their seeds in turn was measured. It was found in brief, that there was no difference in their average size. The seeds from the small parent seeds were just as large on the average as those from the large parent seeds.

Such a result, it may seem, is contrary to all our experience. Do not the taller children in the family tend to have taller offspring? To be sure they do.

[1] By Johannsen, of The University of Copenhagen.

But we must be careful to distinguish between two causes for variations within a family. One is due to hybridity on the part of the parents, a source of variation which is well recognized by breeders and which they avoid by not crossing one stock to another of different type. Any breeder knows that the cross would produce hybrids and that hybrids do not have uniform progeny. It could not very well be otherwise; for the hybrid has received from one of his parents genes of one type, from the other genes of another type, and accordingly he transmits to some of his offspring the one, to others he transmits the other type, and to still others he transmits various combinations of the two. The offspring of hybrids are varied on this account; they do not all receive the same kind of genes from their parents. This fact applies with especial force to man, for man is one of the most hybrid of all species; and children of the same family differ in regard to eye color, hair and many other traits because of the hybridity of their parents. Their sizes vary for the same reason. No two start out life with the same hereditary equipment; the hybridity of their parents makes uniformity among them impossible.

In the case of beans, however, this source of variation, the one due to hybridity on the part of the parents, is excluded. For it so happens on account of their mode of reproduction that bean plants are not hybrids. They reproduce by a process known as self-fertilization. Any one plant is both male and female parent of all its offspring. It seldom crosses with any outside stock. It inbreeds in the strictest possible fashion. Its ancestors have also been inbreeding. For this

reason the bean plant is of pure type rather than hybrid. All of its offspring begin life with the same hereditary equipment. But some are more favored by their environment than others; they receive more food, have a better position in the pod, etc., and they develop into larger beans. Their increased size is actually an acquired trait and should pass on to their offspring, if acquired traits are inherited. But very careful measurements show that the increased size in one generation is not passed on to the next.

It might of course be asserted that the increased size was not given enough of a chance to impress itself upon the race and that if the experiment had been conducted over several hundred generations or more, some effect would have been produced. We are, however, concerned just now with the experimental evidence. The work on beans represents the most crucial series of experiments that we have up to the present bearing on the question of acquired traits and their inheritance. This work was conducted on a very extensive scale and involved measurements of the most exacting nature. Its results are especially valuable because they are free from all possible source of error, in particular from the confusing effect of hybridity. So far as we can see from these experiments an acquired trait brings about no inheritable change in any one generation. Whether or not it could produce any such change in the course of a hundred or a thousand generations is a matter of pure speculation.

It is true that there are some cases in evolution that superficially suggest an inheritance of acquired characteristics, the darkening of a race in the tropics, the

loss of eyes in dark caves, etc. But all of these cases are susceptible of explanation on the mutation theory. They in themselves really furnish no more evidence for one view than for another. It is in fact these very cases that we are trying to account for. An explanation which accounts for them on the basis of known facts is far preferable to one which is purely speculative. Up to the present, mutations are the only kind of hereditary change for which we have definite evidence and so long as this is the case we must confine ourselves to them in explaining the course that evolution took.

Belief in the inheritance of acquired characters rests on an old conception of heredity in accordance with which the reproductive cells were the products of particles that came from the various parts of the body and that were transmitted through the blood stream. It was supposed that there were particles of a particular kind each from the muscles, nerves, etc. The reproductive cells were conceived of as a sort of little house of representatives. If for example the muscles of a person had been well developed by exercise the muscle particles would on this view be well represented in the reproductive cells and the offspring would be born with better muscular development than if the parent had not developed his muscles. In brief, the material from which the next generation developed, the germ plasm, was regarded as a product of the body (the soma).

According to the more modern view of heredity, the chromosomes and the genes contained within them are the material basis of inheritance and constitute the germ plasm. The chromosomes are contained within all cells of the body including the reproductive organs.

They originate in just one way: by the growth and division of pre-existing chromosomes, a process which takes place when a cell divides and forms new cells. All the chromosomes of the body are descended in this way from those of the fertilized egg, the cell with which the individual begins his development. The chromosomes of the fertilized egg, in turn, are derived from the reproductive cells that produced it, the egg of the mother, and the sperm cell of the father.

The fact that the chromosomes are the material basis of heredity makes an inheritance of acquired characters practically impossible. The hereditary particles (the genes) are not built up in each generation by the body and sent to the reproductive cells, as the older concept had it, but they are continuous with each other from one generation to the next through the processes of heredity and reproduction. By heredity, they are transmitted to us from our parents; by growth and reproduction they increase in numbers and populate all the cells of our body as we develop. The most peculiar thing about a gene is that it can reproduce. It can make two genes, each exactly like itself, through the process of growth and division. It does not as a rule change from one generation to the next.

"But," you may object, "surely the genes are not little gods, totally unmindful of their surroundings and free from all outside influences." Your objection is well taken, but it by no means follows that the character of the genes is constantly changing in direct response to bodily changes. A gene is dependent upon the body for just one thing: for its nourishment and other conditions necessary for its growth. If these

conditions are not right the gene simply dies as a rule; it rarely changes its nature. When it does, we have a mutation.

Unless there were something which maintained its identity from one generation to the next, there could be no human race nor any other distinctive form of life. We resemble our parents because we have the same kind of genes as they. We come to have them through inheritance.

There is another matter that must be considered in this connection, concerning what it is that we inherit. We do not really inherit from our parents their blue eyes, their skin color, or any other body characteristics. None of these things are contained in the fertilized egg. What we really inherit are genes. *We do not inherit traits; they develop.* Under a given set of outside conditions, the traits which develop are determined by the genes. Change the environment and you change possibly the course of development and so produce an acquired trait as when you go to the tropics and get a tanned skin. But you do not necessarily change the nature of the genes themselves. With a return to normal conditions development is again of the usual type because the genes have maintained their identity during the interval. In brief, traits are an offshoot, so to speak, of the germ plasm in each generation (see Fig. 30). They do not make the germ plasm. Acquired traits in particular are not inherited, because traits in general are not.

It is of course conceivable that chemicals produced by the body might reach the reproductive cells and cause changes in them, but it is highly improbable

that acquired characters could be inherited in this way. Take an analogy to illustrate the difficulty involved. If pigment diffused from a colored screen, let us say one that is yellow, it would not necessarily combine chemically with the carbon of an arc lamp that illuminated it and permanently change the character of the lamp (corresponding to mutation). Even if such chemical combination did take place, the new compound formed between the pigment and the carbon would not necessarily produce a yellow light. There is no relation

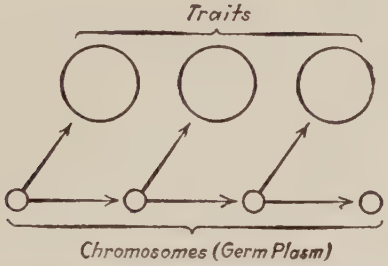

FIG. 30. Diagram to show relation of chromosomes to traits, from generation to generation.

between the color of a substance and the color of the light that it gives off when heated. Thus, common salt, itself white, gives off a yellow light when heated in a flame. For the same reason a gene which had been altered by a chemical substance would not necessarily cause a new trait to develop in such a way as to imitate in appearance an acquired character, even if the acquired character were the source of the chemical substance. Furthermore, there are thousands of genes in a reproductive cell. It is highly improbable that a chemical substance coming, let us say, from a tanned skin, should pick out the particular genes concerned

with skin color and cause just them and no others to mutate.

It is of course conceivable that a tanned skin itself is produced not directly by the sun, but through the agency of some chemical substance which the cell produces under the influence of the sun's rays. It might be contended that such a substance might cause the reproductive cells to develop pigment just as it did the skin cells themselves. According to this view, tanning represents a mutation, or some permanent hereditary change in the skin cells. But we know it is not a mutation; for if a tanned person protects himself from the sun he loses his tan, a thing which would not happen if his skin cells had really mutated. His skin cells should, in other words, behave like those of a brunette. But this they do not do. When a person with a tanned skin returns to the ordinary environment, his skin again becomes white; it has not undergone a permanent hereditary change. Tanning therefore does not represent a mutation in the skin cells and any hypothetical substance which might cause tanning could not very well produce mutations in the reproductive cells if it did not produce them in the skin cells themselves.

It might, however, be urged that the reproductive cells are more susceptible to all sorts of influences than are the ordinary cells of the body and that they might mutate or undergo hereditary changes when other cells did not. There are reasons for believing that this is not true. Mutations do occur in cells outside of the reproductive organs. This fact is shown especially well in plants. The navel orange arose by a

mutation that occurred in a branch of an ordinary orange tree. The mutation took place probably in just a single cell of the young branch, when the branch was still a bud. But the mutated cell grew into the entire branch by the process of cell division and growth. Millions of navel oranges were derived from this one branch by grafting and in fact from the single cell in which the mutation originally occurred. Several other varieties of horticultural plants originated in the same way. Growers of plants refer to mutations of this type as "bud sports," from the fact that they occur in ordinary buds rather than in the flower and its reproductive organs in particular.

Mutations have been observed to occur outside of the reproductive cells also in animals, especially the fruit fly, Drosophila, which has been very closely studied in the laboratory. A fly has been found with one eye red, the normal color for the species, but the other one white, and to all appearances just like the white eyes of a race which arose by mutation. The white eye of the fly in question was probably due to a mutation which occurred when the fly was rather young, in some one particular cell. As the fly developed and grew larger the mutated cell multiplied and formed a patch of tissue which included the eye on one side, but not the eye on the other side. Mutations of this sort have been observed on several occasions in Drosophila. They are referred to as "mosaics" and correspond to the "bud sports" in plants.

Animal mosaics do not as a rule transmit a mutation to their offspring, unless it so happens that the reproductive organs are included in part at least in the

area that arose from the mutated cell. The mutation, however, persists as long as does the tissue in which it is included, and it spreads by cell growth. Its existence terminates only when the tissue itself dies. If the tissue in question should happen to be outside the reproductive organs, it could naturally not continue its existence after the animal itself had died. But in the case of plants, it is possible to detach a branch from a parent plant and to get it to grow into a new one by grafting it on another plant or sometimes by simply planting it in the soil, a process known as asexual reproduction. In this way a mutation that occurred in an ordinary cell of a plant, say in one of its branches, might continue its existence indefinitely.

In animals, however, only those mutations that take place in the reproductive cells can continue their existence after the death of the parent because they are located in the only cells that can detach themselves from the parent and continue their existence in the form of the offspring. From an hereditary standpoint there is really no sharp distinction between the cells of the reproductive organs and those of the body generally. All cells typically contain a nucleus and the nucleus contains the material basis of heredity, the chromosomes, within which are the ultimate units of heredity, the genes. The germ plasm, in brief, is not confined to the reproductive cells; it is within the nucleus of every cell, and wherever the germ plasm is, mutations can occur.

This, you may say, opens up again the door to acquired characters, and the possibility of their inheritance. If the germ plasm is right in the skin cells

themselves, then why not regard it as having changed when the skin becomes darker under the influence of the sun? The fact is, however, that the tanning of the cell does not involve a permanent change in the nucleus. It involves a disposition of pigment granules in the substance outside of the nucleus but no change in the genes themselves, no mutation. The cell has not changed to the brunette type and cannot retain its darker color apart from the direct action of the sun. If a mutation should occur directly in the skin and make it darker it would be just as apt to occur in an unborn child and in the darkness of his mother's womb as in the blazing sun of a tropical beach. Moreover such a change might not be very evident at first. If it were a recessive mutation, it would as a rule not show at all at the time of its occurrence. If it were a dominant it could show immediately, but it would probably manifest itself, not as a general darkening of the entire skin surface, but as a darker blotch of skin in a very circumscribed area, possibly just the size of a mole, or even less. For the mutation would occur, not in all of the skin cells, but probably in just one of them. If now this particular cell did not multiply and form more skin cells, the mutation would not spread; it would be limited to the microscopic dimensions of the single cell, the place of its original occurrence. But should the cell reproduce through division and growth, then the area affected by the mutation would grow in size.

During the early stages of a person's development, the cells are undergoing rapid growth and a mutation that took place at this time would spread over a rather

large area. If the mutation should occur at an extremely early stage in development, when the embryo was microscopic in size and consisted, let us say, of just 4 cells, then a considerable portion of the body, about a quarter, would receive the mutated gene. One that occurred at a later stage would be limited to a smaller area. In either event the mutation would be confined to the cell within which it arose and to descendant cells produced by cell division. It would not be carried over to the reproductive cells, nor to the offspring of the next generation, unless the reproductive cells happened to be included in the mutated area, or rather the area derived from the mutated cell.

It would be an extremely rare occurrence for a gene to mutate at the right time and place in the developing embryo so as to produce a person whose skin was patched. The mutated gene moreover would have to be a dominant. Accordingly a person whose skin was spotted through mutation would seldom or never be seen. But in some plants, dominant mutations do sometimes occur that produce a mottled flower color. You have probably seen such flowers in gardens or florists' shops; the "four o'clock" is a plant that shows it. Not all mottled or striped flowers are due to mutation; but in those that are, such as the four o'clock, it so happens that a certain gene mutates rather frequently and produces red spots on a flower that is otherwise white. Each red spot came from a single cell in which a gene mutated from the ordinary white type to the red. The mutation took place when the flower was still in the bud; and the cell in which it took place had time to multiply and produce a patch

of cells. The mutation too was a dominant, so that it showed immediately in the patches of cells.

A mutation that affects the skin of a person does not by preference arise in the skin. It might, so far as we know, have its origin in any cell of the body that still possessed its nucleus and a full set of chromosomes. A cell of the brain or of any other part of the body does as a rule have a full set of chromosomes and genes, including those for skin color. But if a skin color gene should happen to mutate in the brain, the change would not become manifest, because skin color genes normally do not manifest themselves through any developmental influences on the brain. Neither could the mutation be inherited by the next generation. On the other hand, when a mutation happens to take place in a reproductive cell, or in a cell that is ancestral to a reproductive cell, then, and only then, can it be transmitted to later generations and become manifest in them.

Why the mutation should arise in the first existence in just a particular cell and not in the numerous other cells that surround it, all apparently under similar conditions, is a thing we do not know. The causes of mutation seem to be hidden within the narrow limits of the cell boundary. They are not to be found in the body changes that are obvious to the naked eye.

For body changes of one generation to cause similar body changes in the next would involve a control on their part over the machinery of inheritance that was almost supernatural. It is to be sure remarkable that genes can determine developmental processes and the character of the full grown adult. But the genes

acquired these powers during a long evolutionary process, involving millions of years. Their history is in fact the history of the race. That they should spring into existence almost over night and in direct response to body changes is well nigh inconceivable. It is just this sort of thing that is implied by an inheritance of acquired characters. Moreover, if there were such a thing as this, it would mean that we knew exactly why animals and plants of different kinds come into existence. A strong muscular species would owe its origin to exercise on the part of its ancestors, a species that is quick to constant running, etc. The problem of evolution is not so simple as all this. But it might be asked, "Is it not an equally naive solution to say that species owe their origin to mutation?" Not exactly. The mutation theory makes no attempt to state the causes of hereditary changes; it merely states their nature and affirms that racial changes are at bottom mutations.

What the exact causes of mutations may be, is a problem for the future. We know that mutations do not arise by magic in response to the needs of the species. All the evidence we have shows that species acquired them in the course of a long and painful process. The process itself was slow. And even after many mutations had appeared in the lapse of ages only a comparatively few were chosen. For the mutations that represented changes for the better were extremely rare, probably only a small fraction of the total number. By far the larger portion of them were changes for the bad, for weakened vitality and idiocy rather than greater strength and increased mental powers. But in a state of nature where there was free competition, the

weaklings were weeded out and only the strongest survived. It is for this reason that the human race is comparatively free from idiocy and other defects. Every other species has had the same evolutionary history. The bad mutations failed to be transmitted to future generations; not because they were incapable of transmission to the offspring, but rather because they were weeded out almost as quickly as they arose. Had they received special care in being reared and had they been exempted from competition, they could have lived to reproducing age and left offspring of their own defective type, just as idiots do to-day. And in a comparatively short time, the race would have been loaded down with all sorts of defects, simply because the bad mutations greatly outnumbered the good in point of frequency with which they arose.

Mutation itself is a perfectly random process in the sense that it produces many more changes for the bad than for the good. This is apparent from a study of the process as it takes place to-day, under observation in the laboratory. The same thing was probably true in the past; there is no reason for believing that the nature of the mutative process itself is any different now from what it was during the millions of years that marked the evolutionary history of any species.

The fact that animals and plants usually have the traits that they need in their environment has given rise to the mystical notion that the need of a new structure directly causes its development in any species. What really takes place is that mutations of all sorts make their appearance and any that happen to be of the sort that the animal needs are preserved and

accumulated. The need of a new mutation is by no means the cause of its appearance. Need merely helps to preserve a mutation once it has made its appearance.

It is true that when we examine animals and plants as they exist to-day, in their perfected state, we notice that they have just the things they need for their particular mode of life. But bear in mind that we are coming upon the scene after the selective process has been in operation. We see only the successes. We do not see the countless failures that are strewn along the path of evolution. If we could see them too, we would be impressed not by the perfection of nature, but by its imperfection. We would see thousands of bad mutations for every one that was good. Not that animals in the past were constantly being born with defects. Mutations then were as rare as now; most offspring in any family were like their parents. But when they did depart from the parental type, they changed for the bad as a rule. In the course of ages, there were many such departures. It was only the rare exception that was a change for the better. But when it did turn up it was retained by the species, for the descendants that received it had an advantage over the inferior types, and in the course of time gradually displaced them.

Such was the origin of the race. At bottom, the evolutionary process is mutation. The evolution of a species is the accumulation of mutations. The particular kind of mutations that were accumulated in the past depended upon the mode of life of the species and its environment. For an animal like the frog, that lives in the water, the lucky mutations were those that made

for webbed feet, a slimy skin, and other traits suitable to the environment of the animal and its particular mode of life. In the evolutionary history of man, on the other hand, living in the open and under a large variety of conditions, mutations that made for superior intellect and dexterity were most useful. Accordingly the two species, frog and man, evolved along distinct lines — mutations of a different type were accumulated by their ancestors.

When we compare the two species, we are apt to be impressed by the fact that each has responded to its environment by acquiring a particular set of traits. It appears at first sight almost as though there were something peculiar about each animal's life that tended to produce mutations peculiar to it. Life in the water it might seem, causes webbed feet, life on dry land nimble fingers, free of webbing. But there is really no evidence that the environment has any such specific action on mutation. On the contrary, closer study of the process indicates that mutations of the most diversified types arise in every environment. Human beings, for example, are sometimes born with webbed hands and feet, a fact which would indicate that there was nothing peculiar about conditions in the water that led to this type of mutation, peculiar in the sense that the same conditions were not also found on land.

When we examine species as they exist to-day we are apt to be oblivious of the long and tedious evolutionary process that made them what they are. We forget about the frightful number of failures that went by the board, the mutations that never came to anything. Such would have been the history of any species,

regardless of the environment in which it lived. To be sure environment did play a part in the evolution of every species. But we must always be on our guard in distinguishing between its role as a *selective* agent, and its role as a *causal* agent. An aquatic environment could, through its selective action, bring about the evolution of webbed feet. It would do this merely by causing mutations of this particular type to be retained and accumulated. But whether or not it actually caused the production of such mutations, is another matter. We have no evidence that it does. Conceivably there is some external agent that causes mutations for webbed feet, but it is not necessarily the water itself. Just what it is, we do not know. If light, moisture, and various other environmental factors are causes of racial change it does not necessarily follow that light causes a darker skin to be inherited, that moisture causes webbed feet, etc. The environment is not the same in its action as a causal agent and as a selective agent. Exactly what effect, if any, the various external agents have on heredity is a thing we are ignorant of. In brief, the specific causes of mutations are unknown.

It may now be asked whether there is not possibly some inherent tendency in living substance that made it evolve along certain lines, more or less regardless of the environment. There is in fact a theory, known as orthogenesis, that living substance is limited to certain definite lines in its capacity for evolution and that it evolves along these lines in a sort of predestined fashion. The theory is based purely on evidence from fossils. Let us take a case which has been advanced in support

of the theory. There are fossil remains which show a series of stages in the evolution of a snail beginning with a shell that was not at all spirally twisted to one that was very much so. No particular value could be attached to the twisting of the shell and this was looked upon as evidence for the theory in that it indicated that there was some inherent tendency towards the twisting process. The inherent evolutionary tendencies which the theory postulates would, it was supposed, express themselves even if they produced something that was harmful and led to the eventual destruction of the species. Supporters of the theory offer as evidence for such a harmful tendency the case of a certain extinct animal known as the sabre-tooth tiger. The two upper canine teeth of this animal had become so large that they reached way beyond the lower jaw. From this fact the conclusion was drawn that the canines had become so long as to be not only useless but even to be in the way when the animal opened its mouth, and that the species went out of existence on this account. It looked as though the tendency towards longer teeth had to express itself in the evolution of the sabre-tooth tiger even though it led to the eventual destruction of the species. But careful study of the animal's jaws has shown that the sabre-tooth tiger could open its mouth to an enormous extent. The long canines probably acted as knives in cutting gashes into the prey of the animal and did not offer any obstruction to the action of the jaws. What it was that caused the species to become extinct is unknown; it certainly cannot be reasonably asserted that an inherent tendency towards longer canines was the

cause. The case of the sabre-tooth tiger can therefore not really be offered as evidence in support of orthogenesis.

The theory, in fact, is largely speculative. It contradicts all that we know about mutations, especially as shown by the careful studies made on the insect Drosophila. In this animal, it was found that mutations did not tend to take place in any particular direction. When for example a number of successive mutations affected the wings of Drosophila, they did not all tend to make the wings longer, or shorter, or to bring about any other particular series of changes. But rather were the mutations of all sorts; some made the wings shorter, some caused them to bend up or down, still others led to a dropping out of the veins, or to a change in the shape of the wings, their texture, etc. Mutations, in a word, were found to be "random" in direction. If in a state of nature the wings did change in some particular direction, for example if they became shorter by a series of mutations, this would come about simply by the selection of such mutations as happened to lead to a shortening of the wings. Mutations of other kinds would also take place, but only those that led to the shortening of the wings would be selected, provided the evolution of the wings were restricted to this particular channel.

In a state of nature, however, the mutations that made for shorter wings would be selected only if such mutations happened to be of value under the particular conditions of the species' existence, say on a windswept island, where shorter wings would tend to prevent the flies from remaining in the air too much and being

carried to the sea by the wind. The animals with shorter wings would then have an advantage over mutations of other types and they would gradually displace them under competition. In brief, natural selection would have been the agent which caused the rejection of the various other mutations which also occurred but which were useless.

If there were such a thing as orthogenesis, it would take place entirely apart from natural selection. At any given stage in its evolution, all members of a species would be alike — they would all be expressions of the same inherent tendency. For natural selection to operate, there must be individual differences; some members of the species must be more fit than others, otherwise there is nothing from which to select. Orthogenesis would make possible the evolution of harmful traits if these happened to be the expression of an inherent tendency. If, on the other hand, natural selection operated, distinctly harmful traits could not evolve, for the good mutations would get the better of the bad in competition with them.

Before a series of fossils can be offered as evidence in support of orthogenesis the series must show the evolution of some trait which is either useless or harmful. The evolution of a trait that is useful may have taken place under the guiding influence of natural selection; and if natural selection had operated it would imply that mutations of all sorts were produced during the evolution of the trait, and not simply variations along one particular line that represented the expression of a hypothetical inherent tendency. The evolution of a useful trait is therefore not necessarily evidence for

orthogenesis. It is only when it can be shown that some distinctly harmful trait evolved that we have evidence for orthogenesis, for it can then be argued that some inherent tendency had to have expression. Here lies the difficulty in the way of getting evidence for orthogenesis. Before we can pronounce some trait harmful we ought to be thoroughly familiar with the habits of the species with the trait in question. This is obviously difficult or impossible for species that lived possibly millions of years ago and for which we have only fossil remains, often fragmentary at that. The theory of orthogenesis depends for its acceptance not so much upon our knowledge of certain facts as it does upon our ignorance of them.

The fossils of extinct races are very valuable in telling us about the life of the remote past, but they give us very little information about the precise manner in which a race changes. Take, for example, the evolution of the horse and the fossil remains that have been found of it. There is a series of remains which connect the present day horse with a very small ancestor, about the size of a cat. This series of fossil remains shows, among other things, stages in the evolution of a taller, swift-running type. The number of steps shown is fairly complete, but the whole process took millions of years, and a very long time elapsed between even any two consecutive stages for which we happen to have remains. It may appear as though one stage gave rise directly to the next one, but as a matter of fact there may have been various "futile" side branches none of which ever became sufficiently abundant to leave any traces of their existence in the form of fossils; and in

fact, it seems almost certain that in the long time that elapsed between one stage and the next there must have been many mutations which never even went as far as side branches, and which for the most part were useless.

If we examined some line of evolution as shown by a series of fossil remains, we could get little or no evidence of all the side lines from the series, much less could we get evidence of all the useless mutations which disappeared almost immediately after they arose. The fossil evidence could at best give us a picture of the general sweep of evolution; it could not show us in detail the mutations which arose during the process. In order to see mutations it is necessary to make a very close study of *existing* animals or plants.

In summary, three theories have been advanced regarding the origin of new types: (1) the mutation theory, (2) the theory that there is an inheritance of acquired characters, (3) the theory of orthogenesis. All three theories cannot be correct. In fact each one excludes the possibility of the other two. The evidence discovered by the student of heredity favors the mutation theory. This theory implies that the chromosomes and the genes they contain are the physical basis of heredity and that new types make their appearance because of changes in the genes. If this theory is correct, acquired characters cannot be inherited, because the mechanism of inheritance through chromosomes would not permit of any inheritance of acquired characters. The mutation theory also makes untenable the theory of orthogenesis, according to which changes take place along predetermined lines, and not in all directions as demanded by the mutation theory.

So much for the past. How about the present and the future? Various influences play upon the human race to-day which our ancestors knew nothing about. There are the highly artificial conditions of a modern industrial society. Hordes of workers pour into mine and factory only to emerge bent and stunted in growth. Will their descendants in time be a race of hunch-backs and dwarfs? The printing press has brought with it our spectacles, and a changed diet of soft and easy food our false teeth. Are we becoming a race of beings with false eyes and false teeth? Then there are the numerous drugs, especially alcohol, and many diseases which have come with civilization and crowded conditions.

Can the human germ plasm escape all of these highly artificial influences without a scratch? Our answer to this question depends largely upon the nature of the changes with which we are dealing. No amount of bending could make the race permanently bent. We are dealing here obviously with an acquired trait. Neither could close application of the eyes make the race permanently near-sighted. But in the case of near-sightedness, there is a complication to consider. A person with defective eyes did not necessarily acquire this trait through reading or other close work. He, or one of his ancestors may have been a mutant. It is his good fortune that he was born in a day when spectacles make it possible for him to compete on almost even terms with normal persons. This very circumstance, however, also makes it possible for the mutants to spread; and it may be that near-sightedness is on the increase not because it is being handed down to

the offspring by parents who acquired it through close work, but because the mutation is being handed down and is being spread through reproduction. Such in fact, is definitely known to be true of feeble-mindedness, a defect that is not due to the maddening pace of modern social conditions, as has often been claimed, but that is due entirely to mutation. The rapid increase of feeble-mindedness that we are now witnessing is due to just one thing, namely the rapid spread of the mutation through reproduction. The feeble-minded are actually reproducing at a faster rate than the population in general. What, now, caused the mutation in the first place, is something we know nothing at all about. It would be mere idle speculation to say it was due to modern social conditions. Probably the mutation arose just as frequently in the past as now, but a continuous and vigorous process of elimination prevented it from spreading among our ancestors, a process which is not occurring to-day because the feeble-minded receive special attention and so live to reproducing age.

Up to this point, then, we are dealing with no special circumstances in modern industrial society that would seem in themselves to produce destructive racial changes, racial in the sense that they are permanent from one generation to the next. But now we come to drugs, and in particular alcohol. Here, one is almost bound to believe, is something that must surely produce some injurious racial change, particularly since the drug gets right into the blood stream and reaches the reproductive organs directly. In fact, some experimental evidence on lower animals seems offhand to

indicate that alcohol can bring about hereditary defects, but before we consider the evidence in question it is extremely important that we observe one very necessary precaution; namely, that we be sure to distinguish between the possible effects of alcohol on the unborn offspring as it takes place through the mother, and as it takes place through the father.

Alcohol probably causes defects in the offspring when taken in sufficiently large doses by the mother during pregnancy. Experiments on guinea pigs indicate this, and the same thing probably also holds for man. But the defects are not necessarily mutations. The drug acts directly upon the unborn child through the blood system of its mother, and any defect that it produces in this way is an acquired trait, in the same sense that a tanned skin is. It cannot be transmitted to future generations. The fact that the defect was caused before the child was born, rather than after, does not alter its character as an acquired trait.

Alcohol taken by the father, on the other hand, can not possibly reach the unborn offspring directly and can only affect them through some action on the reproductive cells of the father previous to the time of mating. Any defective offspring that it causes in this way might very well be mutations, for it would have produced its results by acting primarily on the genes carried by the reproductive cells. But there is no satisfactory evidence that alcohol causes defective offspring through the male parent. In the experiments on guinea pigs, practically no structural defects appeared in the offspring of an alcohol treated father; that is, when only the father was alcohol treated, and

not the mother also. There were really no inherited defects in these experiments on the male parents that could be traced for certain to the action of the drug. This result was in sharp contrast to what was got when the mothers were alcohol treated and when numerous defective offspring were produced. Any defects that appeared in the offspring as the result of alcohol treatment of the mother were therefore probably due to the direct action of the drug on the offspring and may safely be regarded as acquired characteristics. Such defects do not represent permanent hereditary changes. It is conceivable that mutations might rarely turn up in response to alcohol but we have no idea at present as to just what such mutations would look like. One worker [1], in fact, experimenting on chickens, claims he got stronger offspring by treating the male parent with alcohol; but he explains his results by assuming that the alcohol killed the weaker reproductive cells, leaving only the stronger.

Disease, like alcohol, produces its effects on the offspring through channels other than mutations. An infectious disease can be transmitted to an unborn child in the same way as alcohol, directly from the mother. The child does not have the disease because his hereditary make-up was changed, but because he was infected with the same kind of germ as his mother. The disease cannot be referred to as a mutation. It could only be so considered if it developed as the result of a change in some gene. In this event, the disease would represent an actual hereditary change and not simply an infection. It could then develop in any de-

[1] R. Pearl, of The Maine Experiment Station.

scendant who received the changed gene and in any future generation.

Our modern industrial society then, seems to offer no special conditions which in themselves lead directly to destructive racial changes. There is just one cause for alarm in the present situation: the let-up of the selective process, the process whereby bad mutations have in the past been eliminated as rapidly as they arose. If the race changes for the bad, it will be in only one way, through the preservation and spread of bad mutations. We cannot at present control the conditions that cause racial change; we know very little about these conditions, except in the negative sense that acquired traits are not inherited. But we can direct the future course of human evolution, just as nature did in the past, by keeping the good mutations and discarding the bad.

Just one more word about the causes of mutation. Very recently a biologist[1] performed some very remarkable experiments in the course of which he artificially produced mutations. He used the insect Drosophila as his experimental material and he was able through the use of the X-rays to induce many of the mutations that had previously been observed to arise in the natural course of events. He employed fairly heavy doses of X-rays, enough almost to sterilize the animal and he worked on both the male and the female. He was able, by means of his X-rays, to speed up enormously the natural process of mutation. In one generation and in the course of about 45 minutes application of the X-rays he induced about half the total number of

[1] H. J. Muller, of The University of Texas.

mutations that it had taken other workers many years to find. The mutations did not show immediately in the flies that had been X-rayed. But their reproductive cells were somehow altered, and their offspring showed the effects of the mutations. Just how the X-rays acted on the reproductive cells is not definitely known. Possibly they struck the genes very much as bullets from a series of rifles might strike a mass of pebbles. They seem to have shattered the individual genes or caused changes in their internal structure. The experimenter was not able to produce any definite kind of mutation at will. Neither did he use agents other than X-rays in producing his mutations in the particular experiments that gave such marked results. His work still leaves the specific causes of mutation unknown, specific in the sense that some particular agent might cause some one kind of mutation. Perhaps there are no such specific agents. At any rate, his work is of extreme importance in that it has shown the possibility of speeding up a process that of its own accord is very slow. If his method can be applied to other forms of life, it may be possible to hasten the improvement of cattle, cotton and other useful races. It is true that the method produces for the most part mutations that are useless or even harmful, just as is true of the mutative process in nature; but the method may also produce an occasional good mutation. The practical breeder could then select and propagate the desired mutation. In any event, a good start has been made.

Such is the nature of mutation. It takes place within the microscopic dimensions of a cell, and it may spread by reproduction until it covers the face of the earth.

It is haphazard and blind in its mode of occurrence, but it is the very process through which the wonderful array of life-forms of the past and present has come into existence. It is the only process by which new genes can come into existence; and it is therefore at bottom, evolution itself.

CHAPTER VII

INBREEDING AND OUTBREEDING

When we hear of first cousins marrying, the problem of inbreeding is raised in our minds. We have always heard that inbreeding is not good. Blood relatives, it is assumed, are apt to have defective children. This view has been held since the earliest historical times and to-day there are laws in all civilized countries against marriage of close relatives. Is the traditional view necessarily correct?

If we look to the lower forms of life, we seem to get some encouragement for the feeling against inbreeding. We find that most animals outbreed. This fact is very clearly shown in connection with hermaphrodites, animals that are both male and female, such as snails and earthworms. These animals produce both sperm cells and eggs, but they seldom fertilize themselves. Some of them are, in fact, incapable of self-fertilization, either because their reproductive cells, male and female, ripen at different times, or because the cells of the same animal for some unknown physiological reason are incapable of combining. Self-fertilization would represent the closest possible form of inbreeding, closer even than brother and sister matings. If inbreeding were good, we might expect to find it taking place among hermaphrodites. Then there is the evidence from plants. When corn is grown, it is the practice of the

grower to pollinate the seed-bearing plants with pollen from different tassels rather than their own. If the plants are allowed to self-pollinate they produce inferior seeds, many of them growing into small and defective plants.

All this looks like a good case against inbreeding. But then there is something to be said on the other side. Hermaphrodites — especially plant hermaphrodites — do not always outbreed. That whole family of plants to which the bean and pea belong habitually self-pollinate. The same thing is true of wheat, rye and other cereals. Still these plants are as vigorous as any in the plant kingdom. Consider also the practices of animal breeders. The best breeds of horses, dogs and other domesticated animals are usually closely inbred. The breeder of a thoroughbred race of horses knows that he would lower the quality of his highly selected stock by introducing into it the blood of some outside stock. Thus it appears that inbreeding is not bad after all and the whole situation becomes very confusing.

One of the practical results of the mutation theory and Mendel's principle has been to offer a final solution to this ancient problem of inbreeding. Consider a specific case. Two people marry who are closely related, both of them apparently normal. They have some mentally defective children, feeble-minded let us say. If either or both of them had been defective we would say to ourselves "a case of heredity" and let the matter go at that. But when we find that both of the parents are normal and that they have defective children, we react to the case with somewhat of a

feeling of horror. We feel that there is something peculiarly dangerous about the inbreeding process that leads to the weakness of the next generation. But is there really something in the process itself which is bound to have disastrous results?

First of all, we must distinguish between two types of normal people — real normals and apparent normals. Mendel in working with his pea plants found that there were some plants that produced offspring all like their parents but others which produced another type of offspring in addition to their own kind. The first were pure in the hereditary sense, the second were hybrids. Human beings are like Mendel's peas in this respect. Some are pures, others are hybrids.

An apparently normal person may be a hybrid for feeble-mindedness. He carries an hereditary unit for the weakness, which we can designate as the gene for feeble-mindedness (f). He also carries another unit (F), the dominant normal allelomorph of f. The hybrid is accordingly of genetic composition $\left(\frac{F}{f}\right)$. If two hybrids should mate they might have some idiot children, for the hybrids form two types of reproductive cells, half containing F, the other half f. If a sperm cell should fertilize an egg cell, and if each contained f, then a fertilized egg would be formed containing 2 f's $\left(\frac{f}{f}\right)$ and this would develop into an idiot child. The hybrids may also have normal children, some of them pure $\left(\frac{F}{F}\right)$, others hybrid like their parents $\left(\frac{F}{f}\right)$, depending upon

how the reproductive cells happen to come together in fertilization. In brief, the mating of two hybrids $\left(\frac{F}{f} \times \frac{F}{f}\right)$ gives three kinds of offspring, the pure normals $\left(\frac{F}{F}\right)$, the hybrids $\left(\frac{F}{f}\right)$ which appear normal, and the idiot children $\left(\frac{f}{f}\right)$. These come on the average in families in the ratio of $1\left(\frac{F}{F}\right) : 2\left(\frac{F}{f}\right) : 1\left(\frac{f}{f}\right)$. If we add up the first two terms of this ratio by lumping together the pure normals $\left(\frac{F}{F}\right)$ and the apparent normals $\left(\frac{F}{f}\right)$, we get 3 normals to every 1 idiot child produced on the average by hybrid parents.

Now, normal parents can have feeble-minded offspring only in case both parents are hybrid and then they have offspring in the ordinary ratio of 3 normal to 1 feeble-minded, the simple Mendelian ratio. These facts hold regardless of whether or not the parents are close relatives. In the case of brother and sister matings, however, the chances are comparatively great that if one is a hybrid, the other one also is. From the fact that they have the same parents, there is likelihood that if either one received the gene for feeble-mindedness from his mother or father, the other one also did. In other words if the gene for feeble-mindedness is in the family it is apt to be distributed to several of the children rather than to just one of them. The children now may appear normal, yet a fairly high proportion of them may be hybrids and have feeble-minded children in the next generation, if

they interbreed. The chances are also fairly high that two first cousins might both be hybrids if the idiot gene is in the family, for they have in common grandparents from whom they might both have got the gene.

But suppose that either hybrid, say the man, had married into an outside family. The probability now is much greater that any normal appearing woman that he marries would be, not another hybrid as before when his sister or other close relative was considered, but rather that she would be a pure normal. The hybrids are not anywhere near so common in the general population as are pure normals and any outside person with whom the hybrid mates and who appears normal is much more apt to be a pure normal than is one of his close relatives. To put the thing in symbols the mating of the hybrid $\left(\frac{F}{f}\right)$ to an outsider $\left(\frac{F}{F}\right)$ is represented by the formula $\frac{F}{f} \times \frac{F}{F}$. This mating gives only normal appearing offspring in the ratio of $1\,\frac{F}{F} : 1\,\frac{F}{f}$.

Note, however, that half the offspring from the mating just considered (of the hybrid to an outsider) are hybrids, and that the gene *f* is still in existence. The gene cannot be made to disappear by outbreeding. It is simply "under cover," so to speak. Note also that inbreeding did not cause the production of the gene for feeble-mindedness but that it simply allowed two such genes to come together and to express themselves. Outbreeding prevents this result because it is likely that the "outside" parent will contribute the

gene *F* to all of the offspring and therefore will prevent the feeble-minded condition from expressing itself in any of the offspring that happen to receive *f* from the hybrid parent.

Inbreeding does not allow only bad qualities to express themselves in the offspring. Any good qualities that are dependent upon recessive genes would come to the surface in the same way as do the bad qualities. Outbreeding on the other hand would tend to prevent the appearance of highly desirable, but recessive traits that are rare, because the outside stock would in all likelihood not have the exceptional gene. It would have instead some dominant gene which would prevent the expression of the good gene, just as *F*, introduced by an outside stock into an *f*-containing family, would prevent *f*, a bad recessive gene, from expressing itself.

Up to this point we really have no case against inbreeding. The Mendelian analysis shows that the process by itself does not produce the genes for feeble-mindedness or any other bad trait. But it may seem possibly as though it allowed the bad genes to become more numerous than if outbreeding took place. For example, let two hybrids inbreed $\left(\frac{F}{f} \times \frac{F}{f}\right)$ and produce offspring in the ordinary ratio of $1\,\frac{F}{F} : 2\,\frac{F}{f} : 1\,\frac{f}{f}$. Count up the *f*'s among the offspring and you will find that they form 50% of the total number of genes. Next let the hybrids outbreed with some pure normal stock $\left(\frac{F}{f} \times \frac{F}{F}\right)$ and produce offspring $\left(1\,\frac{F}{F} : 1\,\frac{F}{f}\right)$. Now count up the *f*'s and you find that they form only 25%

of the total genes, instead of 50% as before; and it looks as though the proportion of bad genes had been reduced by outbreeding. But let us not overlook the pure normals and their offspring. Consider the entire population, consisting in this case of two families, one the hybrids and the other pure normals. If we do this,

OUTBREEDING

Family *a*	Family *b*		*Children*
$\frac{f}{F}$	$\times$ $\frac{F}{F}$	gives	1 $\frac{f}{F}$: 1 $\frac{F}{F}$
Total *f*'s = 1 in 4, or 25%			Total *f*'s = 1 in 4, or 25% (no change)

INBREEDING

		Children
Family *a* $\frac{f}{F} \times \frac{f}{F}$	gives	1 $\frac{F}{F}$: 2 $\frac{f}{F}$: 1 $\frac{f}{f}$
Family *b* $\frac{F}{F} \times \frac{F}{F}$	gives	4 $\frac{F}{F}$ (if there are 4 children)
Total *f*'s = 2 in 8 (1 in 4), or 25%		Total *f*'s = 4 in 16, or 25% (no change)

TABLE 1, to show non-effect of breeding method on total percent of *f*-genes in the population.

we find that outbreeding does not reduce the percent of genes for feeble-mindedness (see Table 1). Neither method of mating (inbreeding or outbreeding) has in itself any effect on the proportion of genes for feeble-mindedness in the general population. It is merely in the distribution of the genes that the two methods differ in their effects on the offspring. Inbreeding allows two genes for feeble-mindedness to come to-

gether, outbreeding does not. The reason for this in substance is that in the general population the genes in question (*f*) are greatly outnumbered by their dominant normal allelomorph (*F*). Within a given family that contains the gene, this is not the case. Accordingly, it is unlikely that two genes for feeble-mindedness should come together when two members of the general population outbreed. But when inbreeding takes place there is a bigger chance for the two genes to meet.

The genes for feeble-mindedness could be eliminated from the human race if all persons with them were selected and prevented from having offspring. It is, however, impossible at present to select the hybrids, because they appear normal and are indistinguishable from pure normals. The gene cannot be detected in the hybrid and cannot be eliminated through him. But it can be detected in persons who are pure for it, for they are feeble-minded. In order, therefore, to eliminate the gene, it would be necessary first to get it out of the hybrids and into offspring that are pure for it. It must be got out from under cover in the hybrid and into the pure type, where it is detectable. Inbreeding would greatly accelerate this process. The gene would then be constantly eliminated with the elimination of persons who are pure for it, provided feeble-minded persons were prevented from having offspring.

Inbreeding could assist in the selection for a good trait just as it could in the selection against a bad trait. Any recessive gene that was the basis of a good trait could be made by means of inbreeding to come to the surface if it had been previously concealed by its dominant allelomorph in the hybrid. The good trait would

express itself in persons who were pure for the recessive gene concerned and if such persons reproduced more rapidly than those of inferior types the gene and its trait would spread.

Inbreeding does not in itself favor one gene rather than another even though one is for a good trait and the other for a bad trait. It does, however, tend to eliminate hybrids from the population and to substitute the pure types for them. For example, if a group of people were all hybrid for feeble-mindedness $\left(\frac{F}{f}\right)$ and then started to inbreed, eventually the population would consist of just the pure types $\left(\frac{F}{F} \text{ and } \frac{f}{f}\right)$. The hybrids $\left(\frac{F}{f}\right)$ would all be eliminated, not because they are weaker than the pure types but simply because the inbreeding process automatically brings about a separation of the allelomorphs F and f and segregates them into the pure types $\left(\frac{F}{F} \text{ and } \frac{f}{f}\right)$.

Just how this production of the pure types comes about through inbreeding can be shown best in connection with hermaphroditic plants where self-fertilization, the closest form of inbreeding, takes place. Consider a plant that self-fertilizes, the "four o'clock" that you sometimes see growing in gardens. There are two varieties of four o'clocks, one with red flowers, the other with white. Hybrids (with pink flowers) can be produced by crossing the two varieties. They receive a gene (w) from their white parent and the allelomorphic gene (W) from their red parent, and have the formula

$\left(\frac{w}{W}\right)$. They produce reproductive cells of two types, half containing W, the other half w. This applies to both the pollen (in the male part of the flower) and the eggs (in the female part). When the plant is self-pollinated the male and female reproductive cells come together in the usual way and produce by their chance combination offspring in the Mendelian ratio of 1 red $\left(\frac{W}{W}\right)$: 2 pink $\left(\frac{W}{w}\right)$: 1 white $\left(\frac{w}{w}\right)$.

Consider now what happens when the offspring are self-fertilized. The reds $\left(\frac{W}{W}\right)$ can produce nothing but red offspring and the whites $\left(\frac{w}{w}\right)$ only white offspring. Both of them are pures, and can reproduce only their own type upon being self-pollinated. But the pinks are hybrids $\left(\frac{W}{w}\right)$ and they continue to reproduce offspring in the Mendelian ratio $\left(1\ \frac{W}{W} : 2\ \frac{W}{w} : 1\ \frac{w}{w}\right)$. Half of their offspring are hybrids $\left(\frac{W}{w}\right)$ the other half are pures, either red $\left(\frac{W}{W}\right)$ or white $\left(\frac{w}{w}\right)$. Note now, that in each generation the pures reproduce 100% pures but the hybrids reproduce only 50% of their own type. The other 50% are added to the ranks of the pures. If we began with hybrids only, then in the first generation after inbreeding about 50% of the offspring would be hybrids, in the second 25%, in the third only 12½, etc. The hybrids thus continue to

diminish in each generation and in the course of about 10 generations they practically disappear leaving only the pure types (see Table 2).

The plants with which we began might have been hybrid for many other traits besides flower color. But eventually the inbreeding process would make them pure for all of their traits. Not all of the offspring would have the same traits at the end. They would have them in different combinations. This fact be-

Parent		$\frac{w}{W} \times \frac{w}{W}$		
First generation	$1\,\frac{W}{W}$	$2\,\frac{w}{W}$	$1\,\frac{w}{w}$	Proportion of hybrids : 50%
	Let each plant produce 4 offspring, giving			
Second generation	$4\,\frac{W}{W}$	$2\,\frac{W}{W} + 4\,\frac{w}{W} + 2\,\frac{w}{w}$ (i.e., 8 offspring in all from the 2 hybrids, in the 1 : 2 : 1 ratio)	$4\,\frac{w}{w}$	Proportion of hybrids : 4 in 16, or 25%

TABLE 2, to show the reduction in the proportion of hybrids with inbreeding.

comes evident from Mendel's experiments. When Mendel produced his hybrid peas and inbred them he was able to get all possible combinations of traits among the offspring of the hybrids. For example, from one of his crosses he found that he could get purple flowers to go with either tall or dwarf size of plant and that red flowers could go with either tall or dwarf, so that he got plants with four combinations of traits (1) purple, tall, (2) purple, dwarf, (3) red, tall, (4) red, dwarf. In Mendel's experiments not all of these types were pure

but by continued inbreeding each would have become pure for both flower color and size, or for any other trait for which the original hybrids had genes. The various pure races thus produced, after a period of self-fertilization, are known as "pure lines." Each one reproduces only its own type when it is self-fertilized.

Inbreeding on the part of human beings would have the same sort of result — the elimination of hybrids and the production of pure types. The process would take longer in man, because the marriages of first cousins or even brother and sister matings are not so close a form of inbreeding as self-fertilization. But eventually inbreeding even in its less intense form would do away with the hybrids for the most part and leave a preponderance of pures. If a person in such an inbred population appeared normal you could be pretty sure that he was a pure normal and not hybrid for feeblemindedness or any other trait. His children would develop no weaknesses even if he mated with a close relative, because he would transmit to them only the normal genes. There would in addition be persons in the population who had other combinations of genes, including recessives that made for weaknesses. But they would all or mostly all be of pure type if inbreeding had been taking place for a sufficiently long time, and if they now continued to inbreed, their children could develop no weaknesses except those that were already apparent in the parents. No weakness would crop up that had been hidden in the parents through hybridity. All the offspring would conform to the same types as the parents. The population, in brief, would be thrown into a number of distinct camps, each consisting in

effect of a pure line, and each reproducing only its own type upon inbreeding.

Consider now what would happen if two of the pure strains in the population crossed with each other. Let one strain have a bodily weakness, the other a mental weakness. The chances are that the children from the cross would have the weakness of neither parent but would be strong in body and mind. It has in fact been determined experimentally among the lower forms of life that hybrid offspring are more vigorous than either pure type to which the parents belong. Take corn plants as an example. When two distinct strains of corn are crossed the offspring are as a rule much taller and more vigorous and fertile than either parent.

It might appear from this as though outbreeding produced good results because of some peculiar effect that followed upon a "mixing of bloods." But let us see how the thing comes about. Vigor and fertility are really more complicated than they may seem at first sight. Take vigor in a plant. It may be based upon a big system of roots, upon well developed leaves with plenty of green coloring substance (chlorophyll), upon stout stems, etc. If any one of these traits were lacking the plant would suffer. Vigor has a correspondingly complicated hereditary basis. It is dependent not upon just one gene but upon many, all of which cooperate to produce a strong plant. We can label these genes *A*, *B*, *C*, etc., and the corresponding weak genes *a*, *b*, *c*, etc. Let us limit ourselves to just the first two of these genes. There might be two pure strains of plants, one of which had the genes *Ab*, the other *aB*. Each would be weak because neither has both *A* and *B*. Now cross

the two strains, and you produce hybrids $\left(\frac{A}{a}\,\frac{b}{B}\right)$. These hybrids receive A from one parent, B from the other. They also receive the weak genes a and b, but these are recessives and do not influence the development of the offspring in the presence of the corresponding dominants A and B. The hybrids accordingly develop into strong plants. Had we been dealing with a larger number of genes the result would have been the same, provided each parent had contributed to the offspring some dominant genes that the other parent lacked.

The crossing of two distinct strains does not always cause an increase in vigor. When one of the strains has all the dominant genes, $\left(\frac{A}{A}\,\frac{B}{B}\right)$ and the other none, $\left(\frac{a}{a}\,\frac{b}{b}\right)$ then the hybrid offspring $\left(\frac{A}{a}\,\frac{B}{b}\right)$ are no stronger than the parent with the dominants. The offspring are stronger than both parents only when they have more kinds of dominant genes than either of them. But when two distinct strains are crossed it is very unlikely that one of them should contribute to the offspring all of the dominant genes for vigor and the other none of them. Each as a rule has some that the other lacks. The hybrid offspring have the combined number of the two and are accordingly more vigorous. The mere fact of hybridity could cause no increase in vigor, provided it was not accompanied by an increase in the number of different dominant genes.

It had been known for a long time that the crossing of distantly related strains caused an increase of vigor in

the offspring but it was thought that the crossing process produced its beneficial effects in some mysterious way by a "mixing of bloods." We can readily understand now how the element of distant relationship enters into the situation. Strains that are distantly related have had a different history for a comparatively long time. The two may have been alike in the distant past, when they had the same ancestors. But in the course of time many of their genes became different through mutation. Then too the outside strains with which they crossed during this time were probably different and so they received unlike genes from the outside. Many of the genes that thus came to differ in the two strains probably had to do with vigor. Each strain now has some or many dominant genes affecting vigor that the other lacks. When the two strains are crossed the offspring receive the combined dominants of the two and so are more vigorous.

The good effects of outbreeding are probably due entirely to the mutually complementary manner in which the parents supply dominant genes to the hybrid offspring. It is not known, however, why strong traits are as a rule dependent upon genes that are dominant rather than recessive.

Consider now what would happen to the vigor of a race if it started to inbreed after having outbred. The parents with which we begin have the vigor that usually comes with hybridity. But when they inbreed, they produce a large variety of offspring according to the Mendelian expectation. Not all of the offspring would be hybrids like their parents. Some would be pures; and of these, some would be pure for dominant allelo-

morphs, others for recessives or for some combination of dominants and recessives $\left(\text{as } \frac{A}{A}\frac{b}{b}\right)$. Those that had the recessives would be weaker than their parents and they would pull down the average vigor of the population. In each successive generation of inbreeding, the hybrids would contine to produce some pure recessives. The strength that was due to hybridity would disappear as the hybrids disappeared, and the weaknesses due to the pure recessives would show up instead. In this way the general vigor of the population would continue to decline. But the decline would not continue indefinitely. After a certain amount of inbreeding, about 10 generations of it, the hybrids would all have been eliminated from the population and only the pure types would be in existence. Further inbreeding now could have no effect whatever on the average vigor. The whole process would take a rather definite course depending upon the rapidity with which the hybrids were eliminated. In the case of self-fertilization about half the hybrids are eliminated in each generation, so that the percent of hybrids goes from 100 to 50 to 25 etc., with succeeding generations. If we plotted generation against percent of hybrids, we would get a curve such as shown in Fig. 31. Note that the drop in the curve is rather steep in the earlier generations, due to the fact that in the first generation the absolute drop in percent of hybrids is 50, in the second it is only 25, etc.

The apparently conflicting effects of inbreeding on the vigor of the offspring can now be understood. Most animal species are bi-sexual; that is, the sexes are lodged in separate individuals. As a result largely of

this fact the species outbreeds to some extent at least. They cannot self-fertilize and so they must mate with other members of the species. The offspring of the same family as a rule separate and mix with the general population before they reach maturity and cross with some outside strain. Their parents did the same. As a result the various members of the species are hybrids. Close inbreeding on their part is followed by an initial reduction in the vigor of their descendants.

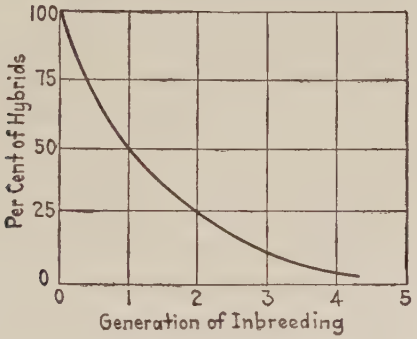

FIG. 31. Effect of inbreeding on percent of hybrids from one generation to the next.

Most plant species are also hybrid, even those in which the sexes are lodged in the same individual, because they habitually outbreed through the agency of insects or the wind. Inbreeding of plants is followed as a rule by the same initial reduction in the vigor of the offspring as in the case of animals.

But plants which habitually self-fertilize form pure lines and the inbreeding of them has no effect on the vigor of the offspring. Such is the case with the various members of the pea family. These habitually inbreeding races have come by the process of natural selection

to have only genes for strong traits; the weaker types were eliminated in competition with the stronger. It is for this reason that they are vigorous; and it is because the process of inbreeding has made them pure that further inbreeding can have no effect whatever on their vigor.

The various highly selected races of horses and other domesticated animals are not so very adversely affected by inbreeding because they, too, have become comparatively pure by the very process of inbreeding. These races at the same time possess a highly selected lot of genes and the only effect of breeding to outside races would be an unfavorable one, from the standpoint of the breeder.

We are now in a position to pass judgment on the relative merits of inbreeding and outbreeding. In a hybrid a recessive gene cannot manifest itself; it is prevented from so doing by its dominant allelomorph. The hybrid is therefore neither hampered nor helped by any traits that are dependent upon recessive genes. For instance, a person hybrid for feeble-mindedness develops into a normal person and is at no particular disadvantage on account of his idiot gene. In a state of nature where there is free competition, the hybrids would not be selectively eliminated in any struggle with the pure normals. In other words the hybrid is not unfavorably subject to natural selection; neither is his idiot gene, because the gene lives as long as the hybrid and is transmitted to his offspring. It continues to be protected against the influence of natural selection in any of the offspring that are hybrid and in all future descendants that are. In each generation, the

dominant normal allelomorph prevents the recessive idiot gene from being eliminated by protecting it from the influence of natural selection.

But when any of the descendants inbreed they produce some offspring pure for feeble-mindedness by the coming together of the idiot genes. Natural selection can then operate against such offspring, since they are feeble-minded; and by eliminating them, it at the same time eliminates the idiot gene. In order, therefore, for the idiot gene to be continually protected against the action of natural selection, it is necessary for the line to be maintained continuously hybrid. An interruption in the hybridity of the line for just one generation is sufficient to eliminate the idiot genes to a greater or lesser extent. So long, however, as the line is maintained continuously hybrid, the idiot gene is protected, so to speak, by its dominant allelomorph.

Such protective action on the part of the dominant allelomorph, however, does not in itself cause an increase nor decrease in the proportion of idiot genes in the population; it simply allows them to hold their own. But it so happens that bad mutations (recessive as well as dominant) greatly outnumber the good. Mutations, in other words, tend to cause a relative increase in the bad recessive genes. If bad mutations do not come under the influence of natural selection, they actually increase *relative* to the good mutations.

The bad types do not arise to any appreciable extent in just one generation, because mutations in general do not arise with any great frequency. But if some line of descent is maintained continuously hybrid over a large number of generations the bad mutations

accumulate. For they are protected from the time of their origin. They are transmitted from one generation to the next not only without any decrease in number but even with an occasional increase from time to time through mutation. Such, in fact, is the course of events in a race that is maintained continuously hybrid.

It should again be emphasized that outbreeding in itself does not cause the actual production of bad recessive genes. It is through mutation that the bad recessive genes come into existence; and it is because bad mutations arise with much greater frequency than good, that the one would soon outnumber the other if natural selection did not prevent such a result. Outbreeding leads to hybridity, and through hybridity to a let-up in the action of natural selection against bad recessive genes.

Consider now the effects of inbreeding on recessive genes. If parents happened to be hybrid for some trait, say feeble-mindedness, they would by inbreeding eventually produce descendants that were pure, some of them pure normals $\left(\frac{F}{F}\right)$ others feeble-minded $\left(\frac{f}{f}\right)$. The recessive would then express itself (in the idiot) and come under the influence of natural selection. That is, the recessive would have to compete with its dominant allelomorph, instead of being protected by it. In this way bad recessive genes would be eliminated. Recessive genes that were good, however, could continue to exist and even to supplant any dominant allelomorph over which they might happen to be an improvement.

In short, inbreeding allows natural selection to oper-

ate on recessive genes; outbreeding does not. For this reason inbreeding has an advantage over outbreeding. But it also has a disadvantage; namely, it does not allow for the introduction of good mutations from outside strains. It is here that outbreeding has its advantage. For two distinct strains may each possess some good qualities that the other lacks and by crossing, that is outbreeding, the good qualities of both parents can be brought together in the offspring. In this way all the good mutations that arise among the scattered members of a race can be concentrated into a single line. It is for this reason that you and I, and the rest of us, contain practically all the good mutations that have arisen in the evolutionary history of the human race.

It nevertheless remains true that outbreeding favors the accumulation of bad recessive mutations and that inbreeding favors their elimination. We see then that each method of mating has its advantage and its disadvantage. For the speedy evolution of a race a combination of the two methods is really the most desirable; namely, inbreeding for the most part, interrupted by occasional outbreeding. In this way recessive mutations can come under the influence of natural selection (by means of inbreeding), and at the same time good mutations can from time to time be introduced into a strain from the outside (by means of outbreeding).

In the pea family is realized the very method of mating that is most advantageous for a species. For peas as a rule shed their pollen before the flower opens and so undergo the strictest form of inbreeding; namely, self-fertilization. But bees and other insects carry

pollen from one flower to another and occasionally bring about cross pollination and the breeding with an outside strain.

In most species of animals and plants there does in fact occur a combination of inbreeding and outbreeding, though not exactly in the same way as in peas. For as a rule the two methods of mating do not alternate with each other but take place at the same time. When a person marries, say a second or third cousin, he is inbreeding to a certain extent and at the same time outbreeding. Even if he should marry a woman whom he regarded as strictly unrelated, he would find upon examining the genealogy of his family and hers that the two had some ancestors in common and that they were related, though perhaps distantly. This inevitable relationship of any two members of the human race or of any other race follows from their evolutionary origin. They are all blood relatives. Such a thing as strict outbreeding is really impossible. There is always a certain amount of inbreeding.

The question then arises, "To what extent is the human race inbreeding at present?" To answer this question, we have to consider separately small communities and large, for the amount of inbreeding varies with the size of the community. In almost any small village there is a considerable amount of inbreeding, especially if there is no shifting of the population. For in such small, stable communities, a person can trace his ancestry back only for a few generations at the most before he finds that some of his ancestors were closely related to each other. Thus, some ancestors of, say the sixth generation back, would be found to be

brothers or sisters of others in this generation. Not necessarily that brother and sister married each other; each of them probably married into an outside family, yet both were included in the sixth generation ancestry of the person in question. The brother and sister who belonged to the sixth generation back would have together just two parents of the seventh generation, not the possible four of two unrelated people.

The close blood relationship of a certain proportion of anyone's ancestors follows from the fact that a person doubles the possible number of his ancestors for each generation that he goes back, in that he has 2 parents, 4 grandparents, 8 great-grandparents, etc. A person living in a small stable community could not have the full possible number of ancestors for very many generations before the figure equalled the total number of people in his community; and he would soon find that some of his ancestors were related to others.

In a large community, on the other hand, especially one with a shifting population, there is comparatively little close inbreeding; the close relatives of a person in the population at large are greatly outnumbered by the more distantly related and the chances that he will marry a close relative are much less than in a small community.

In brief, there is rather close inbreeding in small villages; in large cities, there is more outbreeding. Accordingly there is a relatively great proportion of feeble-minded persons in small villages. It does not follow, however, that the proportion of *genes* for feeble-mindedness is any greater in the one case than in the other. For in large cities these genes are simply

scattered among hybrids for the most part. In villages they are concentrated or rather segregated among the idiots. But there is greater likelihood that a normal-appearing person in a large city is actually hybrid for feeble-mindedness and that he is potentially the parent of idiot children.

The proportion of recessive traits in general whether good or bad should be greater in villages than in cities. In villages there should be a relatively high proportion of persons with exceptional ability of a kind that is dependent upon recessive genes. But persons of ability often migrate to the larger cities and carry away the good genes from the country.

The conclusions that apply to the human race as regards the extent to which it inbreeds apply also to the animal world as a whole. In many species individuals form groups that are more or less stable, as herds of cattle, flocks of birds, schools of fish, etc. The extent of inbreeding varies with the size of the group and its permanency from one generation to the next. Probably many or all such groups are more or less stable, even among animals that wander about a good deal. Birds, for example, return to their old flock when it forms again after breaking up. The young also join the flock. Inbreeding, therefore, takes place in such a "community" just as it does in a small human community. Animals also that do not form groups such as cats, bears, etc., are limited in their wanderings to a comparatively small geographical area. They tend to form what might be called geographical groups (as contrasted to the biological groups above mentioned). Members of the same geographical group inbreed. The

extent to which they do so again depends upon the size of the group. It is possible that in the many instances when animals do not wander very far from their place of birth brother and sister matings or matings between parent and offspring are common. Just to what extent such close inbreeding took place in the early history of the human race is difficult to determine. But primitive man and his pre-human ancestors almost certainly lived at one time or another in very small isolated groups, groups which may not, in fact, have been any larger than the family itself and in which it seems likely that there must at times have been very close inbreeding.

With the introduction of modern methods of transportation accompanied as it has been by the intermingling of peoples and with the growth of cities, the balance has been thrown in favor of outbreeding. Whether things have gone too far in this direction is difficult to say. To encourage outbreeding further by laws against the marriage of first cousins would at least seem unnecessary. One thing seems fairly certain. The outbreeding process has made the human race hybrid to a large extent. The pure Nordic type or any other pure type among human beings is pure fiction. Beans consist of pure lines; they self-fertilize. Human beings do not consist of pure lines; they outbreed too much. Were there any such thing as a pure type then it would constitute a perfectly homogeneous group. The children in a family of that group would all be very much alike, because there is no genetic variation within a pure line.

So much for the general interpretation of the inbreed-

ing process. But what practical suggestions can the Mendelian specialist give to the person who wants to marry a first cousin and who comes to him for advice? Shall he approve of it? The answer depends largely upon a number of things. If examination of the man's family history shows that there is no gene for some seriously objectionable trait in the family then there can be no strong objection to the marriage. In the case of the Darwin family, with its exceptionally good genes, the marriage of cousins was very desirable. But when there is some bad recessive gene in a family there is danger that first cousins may both be carrying it, as hybrids, and they may expect some of the children from their union to be defective. In this case it would be undesirable from their own personal standpoint that they should marry but from the standpoint of the race it would be preferable that they should marry each other rather than some outsiders if they are going to have children. For by marrying to outsiders they simply allow the bad gene to survive under the protection of its dominant allelomorph and to become scattered among the population at large. But if they intermarry they force the bad gene to come from under cover, and if society now sees fit, it can eliminate the bad gene by preventing the reproduction of the defectives who carry it. No brutal measures would be necessary on the part of society to achieve its end. The defectives could be sterilized by a method which would in no way affect the general health or character of the individual, by cutting or tying the ducts of the reproductive organs. The operation, especially for the male, is extremely simple and in case it were performed shortly after

birth but after the appearance of the undesirable character it would not even have the objection on personal grounds that might come later in life.

Whether or not our newer conception of the inbreeding question will have practical applications remains for the future to decide. For the present it will at least be evident that Mendel's discovery has put an end to the confusion of ideas that previously existed on the subject.

CHAPTER VIII

THE GENETICAL INTERPRETATION OF SEX

The romantic relationship between the male and female of man is in many respects peculiar to the human species; yet from a purely biological viewpoint it has the same essential result as it has in other species of animals — the union of the sexes and the production of offspring. These two processes are so intimately associated in man and in all the more familiar animals and plants that it would seem inherently impossible to have offspring without sexual union first. If the question is asked, "Why are there male and female?," the obvious answer might seem, "In order that there might be offspring."

Yet reproduction is not necessarily bound up with sex. In the bacteria and in certain other simple organisms there are neither male nor female; all individuals are essentially similar. Reproduction simply involves the constriction of the parent into two — cell division. Even in some of the higher organisms, especially plants, reproduction may take place directly, without the intervention of two parents. The potato, as is well known, is reproduced by means of cuttings. The banana lacks fertile seeds and must be reproduced by means of slips. Many highly cultivated horticultural varieties are regularly reproduced by means of

grafts. Other examples of the same sort of thing could be given in plants. Among animals there are certain species of worms that chop themselves up into segments and then grow into new worms from the segments. Some of the simpler animals can reproduce by constricting off "buds." All these cases are examples of asexual reproduction, as it is called.

Consider now what happens when an animal or plant reproduces asexually. Suppose you cut off a slip from a geranium and plant it. You cause the twig to undergo a renewed growth. All that happens is that the cells of the twig start growing and dividing again, and so the twig gets bigger and becomes a plant. No sperm or egg cell took part in the production of the new plant; neither was there any fertilization.

Now, the fact that offspring may be produced in this simple way indicates that the union of male and female is not absolutely necessary for reproduction. In fact the simpler method was probably the original one. It was only later in the course of evolution that sexual reproduction came into existence. But this more complicated method of reproduction is at present the usual one. It is a method that is by no means confined to the more familiar animals. Plants ordinarily produce cells that correspond to the sperm and egg cells of animals. The essential part of a seed is a germ or young embryo that grows from a fertilized egg cell.

Even among the simplest forms of life, some of them microscopic in size and consisting of just a single cell, sperm and egg cells or their equivalents combine in forming the new individual. From the fact that this

method of reproduction is so prevalent in the plant and animal kingdoms, we are naturally led to ask, "Of what particular advantage is sexual reproduction?"

Let us get at the answer to this question by considering a few simple facts connected with heredity. In species that reproduce asexually the offspring have just one parent from which they can inherit their genes, not two as in sexual reproduction. It is, therefore, not possible for a mutation to be introduced into one line from some other one. Any individual has just a single line of ancestors, one in each generation; and all the mutations that it has must have occurred within that line. In this respect asexual reproduction has the same disadvantage that continued and exclusive inbreeding has. Sexual reproduction, on the other hand, makes possible outbreeding and allows two strains to come together each of which has good mutations that the other lacks.

Thus it happens that the genes which we contain today are the pick of all the mutations that occurred over eons of time, the time that was consumed in the evolution of the race. They were rare and lucky chances and occurred only here and there among the almost countless numbers of individuals that existed during the evolutionary process. But sexual reproduction made possible the gathering together and concentration of these lucky chances into a comparatively few strains. And the product of it all is ourselves.

There is another advantage which comes with the sexual method of reproduction. So long as animals and plants reproduce by the older method, there cannot be much variety among their offspring. Men who grow

highly cultivated varieties of plants are familiar with this fact. They propagate their pears, apples and plums by making grafts. Their object is to get new plants that are absolutely true to type. When they make grafts, they use the twigs of a plant, not the seeds. The twigs simply go ahead and grow into new plants. The cells in any one twig are like those of any other. They all have the same hereditary make-up. When a twig grows into a new plant, the cells in its buds grow and produce through the process of ordinary division new cells exactly like the old. Thus each new plant comes to have cells that are just like those of the old parent plant in their heredity make-up. Accordingly all plants are uniform in appearance, in the quality of their fruit and in almost every other way. But had the plant grower used seeds instead of twigs, then he would have got a motley array of offspring. He would have found that none of his new plants conformed to the parental type and that practically no two were alike. For if he used the seeds, he would be getting his young plants from the germs, the young embryos within the seeds, and the germs grow not from cells that are of the ordinary sort and that are produced by ordinary cell division, but from the reproductive cells. The seeds in brief grow from the fertilized eggs of the parent plants. It is for this reason that no two are alike in their hereditary make-up.

There is nothing in fertilization itself that leads to variability; no such mysterious thing as might be implied by the term "mixing of bloods." If both parents are of pure type, the offspring will all be of one class, regardless of whether the parents were of the same

"blood," or different. Thus, if one parent is $\frac{A}{A}$ and the other $\frac{a}{a}$, the offspring will be alike in that they will all be $\frac{A}{a}$. But if the parents are hybrid, then they may produce offspring in great variety. For one thing, the reproductive cells of a hybrid are not all alike. They owe their variety to a special type of division (the reduction division) that sorts out the genes in various ways. Then again the reproductive cells come together in many different combinations and produce offspring of many different kinds. This is what happens when the parents reproduce by the sexual method. But in the case of asexual reproduction, all the offspring of a given parent are alike, even if the parents are hybrid. It would make no difference for how many traits the parent was hybrid; the offspring would all be hybrids of the same kind, provided their parent reproduced them asexually — through ordinary cell division and growth.

Now the plant breeders have got plants that are especially suited to the needs of man and for this reason they want them to remain true to type. But in a state of nature, absolute uniformity in the offspring would be of disadvantage to a species, especially in a changing environment. For if conditions should become bad for one they would also be bad for all the rest and there would be danger of the entire race's disappearing. If there were variability among the offspring, there would be a chance that at least some of them would be able to live in the changed environment and so to continue the race.

So far, then, there are two advantages in the sexual method of reproduction: (1) it makes possible the concentration of good mutations; (2) it makes possible genetic variability. It was because of these advantages that sex became almost universal in the course of evolution. For species that reproduced sexually eliminated those that did not, in competition with them.

But sex was not fully developed from the very start. Like everything else, it developed gradually in the course of a long evolutionary process. In the early stages of evolution, fertilization involved merely the union of two cells that were essentially alike. At this stage, there was no differentiation into male and female. Both the parents and their reproductive cells were similar. But gradually the cells of one parent became larger than those of the other and were loaded with food for the young. With their increase in size went a loss in their power of movement. They became the eggs. The cells of the other parent became smaller and highly motile. They evolved into the sperm cells. Their small size made possible their production in large numbers without sacrifice of material. The parents that produced the sperm and egg cells were at first alike apart from the difference in their reproductive cells. It was only later that the two sexes came to differ in bodily form and activity. In the earlier stages the female simply shed her eggs into the water and allowed the young to shift for themselves. But later she retained the young within her uterus. She nourished and protected them even after their birth, as well as before. The female was rendered more or less helpless during such times and was dependent upon the male. It

so happened therefore, that a more or less permanent union was formed between the sexes, and the complex relationships between male and female in man represent the culminating stage in the evolution of sex.

The changes that marked the evolution of sex were probably in the nature of mutations, just as is true of any other trait. Each of the more important stages did not necessarily involve just a single mutation. For example, the differentiation of sperm and egg cells came about possibly through the piling up of a good many mutations. Even the initial stage involving the fusion of the two simple sex cells probably took place through several steps, each a separate mutation. Just what these stages were would be difficult at present to say. But the union of two cells involves the union of their nuclei and a later reduction division, complicated internal changes which might very well have required a great many steps in their perfection. Moreover, before the sex cells had "learned" to combine, they were ordinary cells that reproduced asexually, by simple cell division. The capacity to combine in two's (and so to function as sex cells) may have been acquired gradually. It is conceivable that at first the two cells did not combine with certainty upon coming together and often separated again, but that in the course of time the attraction between them became increasingly strong as mutations of the right sort arose.

In brief the whole process of sex evolution was gradual and involved the piling up of a great many mutations. Nor did simply mutations of the right sort turn up. The wrong, as well as the right sort probably arose, but it was through the action of natural selection that the

one kind was eliminated and the other retained and accumulated.

Some biologists have advanced an interpretation of fertilization other than the one based on genetics. They base their view largely on observations made on some microscopic forms of life that consist each of a single cell. They have concentrated their attention in particular on a one-celled animal known as Paramecium (see Fig. 32, *a* and *b*). This animal can multiply by simple division. The cell constitutes the entire animal, and when the cell divides the animal increases in number. From a single original parent, large numbers of Paramecia can eventually be derived by simple cell division — a process of asexual reproduction. But under natural conditions these animals cannot reproduce indefinitely by the asexual method. From time to time, there occur what are known as "depression periods." At such times, the Paramecia become sluggish, lose their power of division and show signs of loss in vitality. They now come together in two's — they conjugate (see Fig. 32, *c*). After remaining together for a while, they separate with restored "vitality." They again have their power of movement and cell division. Each of the cells that has conjugated divides. Its

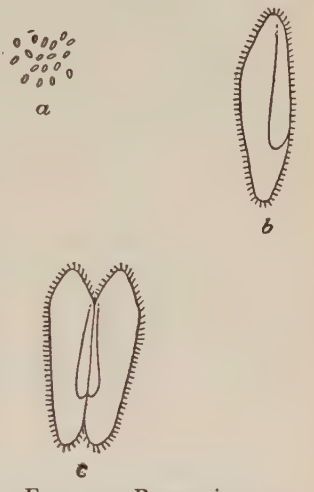

Fig. 32. Paramecium; *a*, several under low magnification; *b*, one more highly magnified; *c*, two Paramecia conjugating.

daughter cells again divide and continue to divide for several hundred generations when the cells again show signs of a depression period and enter upon conjugation.

Certain nuclear changes take place in two Paramecia during conjugation, changes that are the equivalent to fertilization. The nucleus of each Paramecium divides into two (see Fig. 33). One of the daughter nuclei is smaller than the other. It migrates into the other Paramecium with the large nucleus of which it fuses. Thus each Paramecium has a large stationary nucleus and a small migrant one; and these are the equivalent

Fig. 33. Diagrams showing some of the essential nuclear changes during conjugation.

of egg and sperm nuclei. The fusion of the nuclei amounts to fertilization.

Some biologists regard the changes that occur during the depression period as signs of old age, of "senescence" as they call it. They further claim that it is in the nature of all protoplasm to undergo senescence, the same as in Paramecium, and that fertilization is necessary to restore youth — to "rejuvenate" protoplasm, as they put it. Their view is known as the "rejuvenescence" theory.

There are certain objections that can be raised against the rejuvenescence theory. In the bacteria and in certain other primitive forms of life, sex and fertiliza-

tion are not known to occur. Moreover, some cultivated varieties of plants have been propagated over long periods of time uninterruptedly by asexual methods. This fact is known to apply in particular to the banana plant for the reason that bananas lack fertile seeds and cannot reproduce sexually. They have to be propagated by means of cuttings. In organisms that reproduce asexually both in nature and under cultivation, the protoplasm does not undergo senescence; for if it did, they would long ago have gone out of existence on account of old age. The rejuvenescence theory is therefore wrong in so far as it claims that it is in the nature of all protoplasm to lose its vitality through old age. Senescence is not a "property," as it were, of protoplasm. It follows furthermore that the process of fertilization was not made necessary because of some inherent tendency on the part of protoplasm to undergo senescence or because protoplasm had to be "rejuvenated" from time to time.

There is another objection to be raised to the rejuvenescence theory. Nobody has ever shown that the depression period in Paramecium is the same thing physiologically as old age in man. It is true that in both cases the cells have lost their power of growth and division, but there are a large variety of agencies that might be responsible for such an effect and they may not be the same for man in his old age as for Paramecium in a depression period. Moreover, many cells of a young person have lost their power of division; the brain cells, for example, are fully formed (in numbers) at the time of birth and have lost all power of division. We do not regard them as old for this reason. Before we can

speak of old age in a one-celled animal like Paramecium, we ought first to know what the symptoms of old age are in cells generally. Otherwise the term "senescence" is a more or less mystical expression. A similar objection applies to the term "rejuvenescence."

In summary, two objections can be raised against the rejuvenescence theory. (1) There is no evidence that it is in the nature of all protoplasm to undergo death due to old age. (2) The evidence for the rejuvenescence theory rests largely on Paramecium and the view that the depression period in this one-celled animal indicates old age. Definite symptoms for old age are not known for cells, and therefore we do not really know that the depression period in Paramecium indicates old age.

It may, however, be asked what the depression period in Paramecium is, if it is not old age; and why Paramecia tend to stop dividing during this period. The answer to this question is probably bound up with the origin of sex. In the early stages in the evolution of sex, the two cells that fused in fertilization were not only more or less alike, but they were in addition very much like ordinary cells and could in the absence of fertilization reproduce asexually (by cell division). But in the course of evolution the sexual nature of the cells became more pronounced and it became increasingly difficult for them to develop without first undergoing fertilization. The species was, so to speak, "forced" to reproduce sexually; it was given no choice in the matter. The change to forced fertilization took place through mutations. There was a selection and preservation of these mutations largely because the sexual method of reproduction had certain

advantages over the asexual method and because it was of advantage that the species should be forced to reproduce sexually. That is to say, it was of advantage to the species that the sexual method of reproduction should become "obligatory" for it.

The mutations that led to obligatory sexual reproduction produced physiological changes whereby some "block" (or check) was placed on the direct development of the sex cells. The nature of the block did not necessarily have to be the same in different species. Almost any sort of physiological change would do, so long as it prevented the sex cells from developing directly. The egg and sperm cells of man may be prevented in a certain way from developing without first undergoing fertilization. Paramecia may be prevented in another way, when the time of their depression period arrives. We may, therefore, not be able to give a simple answer to the question, "What prevents the egg from developing without fertilization?" There may be one answer for plants, another for animals. The answer may even be different according to the group of plants or animals under consideration, for the block may not be the same in the case of the very primitive as in the higher organisms.

The significance of fertilization or of sexual reproduction may be considered from two points of view, one the genetical, the other the purely physiological. The geneticist can tell us of what survival value the sexual mode of reproduction is to the species, and why it replaced the asexual mode in the course of evolution. The physiologist on the other hand, has still to discover what the nature of the block is that prevents the egg from de-

veloping without fertilization, and the physiological significance of fertilization remains to be discovered. It may not, as above explained, prove to be the same for all species; and probably the physiological conditions that make fertilization necessary at present (the "block") were not the initial cause of sexual reproduction as it arose in the course of evolution.

CHAPTER IX

TWINNING, SEXUAL REPRODUCTION AND REGENERATION

The production of twins in the human race does not indicate, as is sometimes supposed, exceptional virility on the part of the male parent, but is ordinarily dependent upon the female and the production by her of two eggs at one ovulation instead of at two separated by the usual period of a month. Just how the two eggs happen to ripen and get into the uterus at the same time probably varies in different cases and depends upon what is happening in the ovary or ovaries.

The eggs are produced in blister-like swellings, the Graafian follicles, that can be seen on the ovaries. It is usual for one Graafian follicle to swell and burst each month and to release a single egg into the uterus. But it seems likely that occasionally two follicles may mature at the same time, an occurrence that would account for twins in man in the same way as is definitely known to happen in the lower animals. It is possible, by dissecting a pregnant rabbit for example, to find on the ovary the traces of the burst Graafian follicles, the corpora lutea, as they are called, and the number of young developing in the uterus is the same as the number of corpora lutea.

There is evidence, however, which indicates that in rare instances two eggs develop in a single Graafian

follicle instead of the usual one. Two eggs would then necessarily be released into the uterus at the same time, and in the event of fertilization, twins would develop. In brief, twins may be produced in two ways, either by the simultaneous ripening of two eggs in separate Graafian follicles, or (more rarely) by the growth of two eggs in the same follicle.

What has just been said applies to twins of the ordinary kind. But you have probably noticed that some twins resemble each other very closely. They are of the same sex and are so much alike that it is difficult to tell them apart. They are the kind we call identical twins in distinction from ordinary or fraternal twins. Their mode of origin is different from that of the ordinary kind just mentioned.

Identical twins were one at the start. They developed from the same fertilized egg and became two in the course of development. The fertilized egg either divided into two or in some other way gave rise to two parts each of which developed into a complete individual. It is not merely their common origin that makes identical twins alike, but rather their hereditary make-up. The fertilized egg contains certain rod-shaped bodies, the chromosomes, which in turn contain the units of heredity, the genes. Identical twins have exactly the same kind of chromosomes and genes — the kind that the fertilized egg had. They are, so to speak, hereditary duplicates and are accordingly replicas of each other in adult life.

That this explanation for the origin of identical twins is correct is indicated by studies on lower animals, especially the Armadillo. There are always four young

born in an Armadillo litter. They are always of the same sex, and are identical twins, or rather quadruplets. The study of their early development has shown that all four develop from "buds" which are given off from one mass of cells, which in turn are traceable to a single fertilized egg. It is difficult to trace the cell mass in question right down to its microscopic origin, but that it does come from just one fertilized egg is strongly indicated by the fact that in a pregnant Armadillo there is always found just one corpus luteum. Consequently there is probably released into the uterus just one egg before fertilization occurs. All four embryos develop from the one fertilized egg through its growth and budding. It is conceivable, of course, that four eggs come from one Graafian follicle, (the one that gives rise to the corpus luteum), but it is much more usual for only one egg to come from one follicle, even when twins (or other multiple births) are produced.

The membranes that surround the developing embryos give further evidence of their origin. Twins of the ordinary kind are surrounded each by a separate membrane (the chorion). Each developing egg forms its own membrane. But in the case of the Armadillo the embryos have just one membrane in common and so presumably all develop from just one egg.

Among certain insects "identical twinning" has also been observed. In some insects one fertilized egg multiplies and gives rise to three or four hundred embryos, each of which develops into an adult. All the insects that belong to the brood are of the same sex and so far as one can see, all are identical "twins."

Just how one fertilized egg gives rise to two em-

bryos in man is not definitely known. It has been conjectured that the egg divides into two cells in the usual way, but that the two cells now separate from each other and develop, not into left and right half of the body, as they would if they remained together, but that they develop independently, now that they are separated from each other. Each becomes a complete embryo and a complete adult. Possibly the separation of left and right halves does not occur at this very early two-cell stage, but at a somewhat later stage of development. Or it is conceivable that a small mass of cells is produced from the left and right halves of which a bud grows, very much as in the Armadillos, and that each bud gives rise to an identical twin. In any event, the mode of production of the identical twins would be substantially the same; they would have come from a single fertilized egg which by division into two separate parts at an earlier or later stage, or by budding off two separate parts, gives rise to duplicate embryos, the future identical twins.

It has been observed that one of two identical twins is often right-handed, the other left-handed, a fact which may be connected with the probable origin of the twins from right and left halves of the original embryo. The view has also been advanced that a left-handed person is one of two identical twins, the other of whom died very early in his development.

Biologists have performed experiments on lower animals and artificially produced "identical twins." The developing eggs of the starfish and of the sea-urchin, a related animal, have proved useful for such experiments. It is easy to watch the eggs of these animals

under the microscope and to see them divide in a dish of sea water, after the addition of some sperm to the dish. By shaking the water, or with the aid of a fine glass rod, the experimenter can separate from each other the first two cells that are produced by the division of the fertilized egg. Each cell then develops into a complete embryo. A similar experiment has been performed on the frog's egg. In this animal, the fertilized egg divides as usual to produce the first two cells, which ordinarily develop into left and right halves of the body. But if the two cells are separated from each other, each may develop into a complete tadpole — identical twins.

Siamese twins are a special form of identical twins. They both develop from the same fertilized egg, but they do not complete their separation from each other. The extent of the separation varies in different cases. Sometimes the separation is almost complete and there remains simply a small connection between the twins. In other cases there may be two heads and just one body, because the separation of the halves of the embryo involves only the head end. The halves that remain joined develop normally into left and right halves of the body; but the separated halves both complete the missing parts and develop into entire heads. In a similar way other "monsters" are produced, according to the different degrees of separation that take place between left and right halves of the body when the individual is an embryo.

"Siamese twinning" has been experimentally induced in the lower animals, especially fish. The experimenter simply passes a thin thread part way down

the middle of the developing animal, separating left and right halves of the body part way down and keeping them apart for a little while. Each separated half then replaces the missing half. Thus, if the head has been separated into two, the left half of the head grows a new right half and the right a new left half, giving two complete heads.

The production of identical twins has a connection with the healing of wounds. All living substance has the capacity of healing wounds and replacing parts lost through injury — the power of regeneration, as it is called. Human beings have a rather restricted capacity for regeneration; it is limited mostly to growth of new skin over a wound. But some of the lower animals can lose a relatively large part of the body and replace it. Thus, animals belonging to the frog group may regenerate an entire leg that has been lost by accident. A starfish can replace any of its five "arms," should they be torn off. The entire hind end of an earthworm will grow back again if it is cut off. Numerous other examples could be given of the same sort of thing.

The very young embryo, now, has extensive powers of regeneration. If it is at a sufficiently early stage in development, it can repair an injury, so to speak, that involves half of its body and it can replace the lost half. The result then is a case of identical twins, if each half replaces the lost half.

Closely connected with regeneration is a certain method of reproduction possible in some of the lower animals and in most plants. It is a familiar fact that a geranium plant can be reproduced by just cutting off one of its twigs and planting it. The slip takes root

and grows into a new plant. The sex cells of the plant are not involved in this mode of reproduction, which is known accordingly as asexual reproduction. In animals we find the same sort of thing. Simply tear off the arm of a starfish and you make another starfish; the torn-off arm grows into a complete new individual — obviously a case of asexual reproduction. But suppose now that instead of tearing off one of the five arms of the starfish, you had torn the starfish into two unequal halves, one with three arms, the other with two. You would find that the bigger half replaced the two missing arms and you would not hesitate to call this regeneration. You would find in addition that the smaller half replaced the three missing arms and you would again probably refer to this as regeneration and correctly so. But if the smaller piece had consisted of one arm, instead of two, you would be more likely to say that the fragment in question reproduced a new starfish, rather than that it regenerated, although you could still regard the case as a matter of regeneration.

It is evident, however, from a case of this sort that asexual reproduction is substantially the same thing as regeneration. When an animal or plant has extensive powers of regeneration, so extensive that the lost part cannot only be replaced but that the fragment itself can replace what is for it the lost part, then two complete individuals are produced where there was just one before, and we have a case of asexual reproduction. If the smaller of two fragments that regenerates is very small, we usually say that it reproduces the individual asexually, rather than that it regenerates.

All asexually reproduced offspring are in a sense

identical twins. They agree with identical twins in their essential mode of origin: all are derived from one and the same fertilized egg. In the production of identical twins the embryo fragments and regenerates; in asexual reproduction, it is the adult that fragments and regenerates. The same process takes place in both cases, but it simply takes place at a different stage of development.

The similarity in the hereditary make-up of identical twins extends right down to the minute particles that constitute their bodies — the cells. Even here the similarity does not stop. For within the cells are the chromosomes, the rod-shaped bodies that make us what we are by nature. And going still further into the very fabric of the chromosomes we come to the genes, the ultimate units of heredity. It is these genes that are alike in identical twins. To them the twins ultimately owe their similarity. Ordinarily no two persons have exactly the same kind of genes. But identical twins are the exception to this rule. Their cells and genes come to be alike because of their common origin and further because of the way cells ordinarily divide.

The chromosomes, it will be recalled, split lengthwise and line up in the middle of a dividing cell. When cell division is completed and two new cells are formed the chromosome halves have become equally and accurately distributed to each new cell. It is for this reason that the two cells contain a duplicate set of genes. A chromosome contains its genes strung out in single file along its length and the lengthwise splitting that takes place in a chromosome just previous to cell division brings about a duplication of its genes and so a

duplication of the genes in the two new cells. This accurate method of cell division, it will be recalled, is referred to as mitosis. Most of the cells in a person's body are derived from the fertilized egg by mitotic cell division, and are on this account genetic duplicates.

In the case of identical twins we are dealing with two bodies derived from the same fertilized egg and two masses of cells that have the same genetic make-up. The reproductive cells of the twins are, however, somewhat complicated in their mode of origin on account of the peculiar "reduction" division which always precedes the formation of the reproductive cells and which brings about great diversity in their make-up, even in the same person. The reproductive cells of identical twins are therefore not all alike. But all other cells of the body, those of the brain, muscles, etc. — the "body" cells proper, as contrasted to the reproductive cells — all are derived from the fertilized egg through mitotic division only and are duplicates of each other in their hereditary make-up. To put the thing in other words, all unreduced cells of identical twins are exactly alike in their genetic composition because they were derived by mitotic division from the same fertilized egg.

For this reason also, all offspring are alike that are produced by cuttings, by small fragments of the parent, or by any other asexual method. All of their unreduced cells were derived by mitotic division from the same fertilized egg; namely, a fertilized egg that grew into the plant or animal, and that now produced offspring asexually through cuttings or other small fragments. The offspring so produced are accordingly all of the same genetic type — in effect, identical twins.

The production of identical twins is connected with another matter besides regeneration. The embryo is, at an early stage in its development, a rather formless mass of cells, all more or less alike — undifferentiated. What causes some of the cells to develop into arms, others into legs, still others into eyes, ears, etc.? Consider for a moment the very young embryo, at the two-cell stage in its development. One of the first two cells ordinarily develops into the left side of the body, the other into the right side, as happens, for example, in the frog. But separate them from each other, and each cell develops into a complete embryo. This shows that one and the same cell can develop either into just a part of the body or into the entire body, depending upon circumstances. Let it remain in contact with another cell, or other cells, and it develops into a part; separate it from the controlling influence of other cells, and it develops into a complete new individual.

Certain experiments, performed on the frog's egg[1] indicate that the other cell need not even be alive to exert its controlling influence. The experimenter let a frog's egg develop to the two-cell stage and then with a fine hot needle killed one of two cells. He allowed it, however, still to remain in contact with the other cell, which went on and developed. For a while the live cell did not develop into a complete frog, but into a half frog, just as though the other cell were still alive and producing its half of the body. This experiment indicated that it was mere contact which caused each of the first two cells to develop into a half, rather than

[1] By W. Roux, a biologist of the latter half of the nineteenth century.

into a whole individual. It is true that later on in the course of the experiment, when numerous cells had been produced in the live half, some of the cells wandered into the dead half and caused it to grow again (from the cells that migrated in). But nevertheless, the experiment seems to indicate that for a while at least, mere contact did determine that the live cell should develop into a half rather than into a whole, and therefore that contact may be one of the directing influences in development.

But mere contact could not cause a cell to develop into a part of the body if the cell did not have such powers in the first place. The cell, it would appear, is capable of doing a large variety of things in development. It can develop into the whole offspring or it can develop into any part of it. To use a technical term, it is "toti-potent." Its varied capacities are determined by what is *inside* of it; that is by its genes, the hereditary determiners. But the particular path that a cell pursues in development is determined by factors *outside* of itself; in other words, by environmental factors. As the cell mass grows and becomes complicated, the embryo automatically creates within itself correspondingly complicated environmental factors that are different in different parts of the cell mass and that here determine that eyes shall develop, there that arms shall, etc. In brief, the environmental factors cause differentiation.

The view here presented regarding the cause of differentiation is in sharp contrast to an older theory — the "preformation" theory — which conceived of the embryo as existing within the egg preformed in all its

parts — a miniature adult in fact. Development was considered merely an increase in size of the microscopic individual contained within the egg. The preformation theory led to an absurd conclusion; for the embryo within the egg must if complete (and if a female) have contained eggs which in turn contained embryos and so on indefinitely. We now know that the egg is undifferentiated. The cells of the early embryo are also undifferentiated and the experimental evidence indicates that they are toti-potent. The particular path that a cell takes in development would seem to be determined by environmental factors that are in part dependent upon position in the cell mass. This view of development is known as the theory of "epigenesis."

It might be asked in this connection why it is not possible to reproduce a human being from a small fragment of skin or other tissue. For the cells of the skin contain all the genes necessary for the development of a complete individual, and if these cells could be given the proper cultural conditions and their growth stimulated, why should they not, when separated from the body, go right ahead and develop into an embryo? In some of the lower organisms this sort of thing is in fact possible. The living part of a sponge (which is a primitive form of animal) can be broken up into bits by squeezing it through some bolting cloth and if a fragment contains a few representative cells, it will develop into an entire new sponge. In some plants, too, it is possible to get a small bit of the leaf to grow into a new plant.

The reason why such capacity for reproduction is lacking in man is connected possibly with his com-

plicated structure, as shown especially by his individual cells. As the body develops and organs appear, not only do the cells become more numerous, but they also assume special forms — they become differentiated. So long as a cell is simple in structure, undifferentiated like the egg, it has the power of division and growth, and of multiplying. But once it becomes differentiated, it no longer can multiply and grow, especially if it is very highly specialized in structure. A skin cell may still be toti-potent in the sense that it possesses all the hereditary factors necessary for development into a complete individual. But it is nevertheless not capable of such development because of the check that differentiation and specialization have placed on its further growth.

For the same reason man may have lost the power of replacing a limb or regenerating any other extensive part of his body. Some animals, however, have a rather highly complicated structure, as for example some members of the frog group, and still are capable of regenerating lost limbs and other parts. Their cells are just about as highly specialized as man's. It is conceivable that in these particular animals there are scattered among the differentiated cells others that are undifferentiated and from which regeneration takes place. While the animal is intact, the undifferentiated cells lie more or less dormant, but when the animal is injured, the stimulus of the wound may possibly cause them to multiply and grow into a new limb or other lost part.

That there is a possibility of the sort just mentioned is indicated by the peculiar regenerative powers of a

certain thick leaved plant, known as Bryophyllum, that grows in arid regions. Simply remove a leaf from Bryophyllum and you cause the growth of a dozen or so new plants, each appearing with its roots, leaves, and stem in the notches about the margin of the removed leaf. The new plants grow from undifferentiated cells in the notches.

The embryo has much more extensive powers of regeneration than the adult. Comparatively large chunks of tissue have been cut out of a developing frog and have grown back again. Even parts of the nerve cord have been removed and have grown back, parts that would never grow back in the adult. Experiments of this sort indicate that a human embryo also can replace comparatively extensive losses. The greater regenerative power of the embryo is precisely what would be expected on the ground that its cells are less differentiated than those of the adult. Get the embryo at a sufficiently early stage, and its cells are almost entirely unmodified. It is then that one half can replace the other, and that identical twinning is possible.

The precise number of identical twins that can be formed from one embryo varies in different species. Take the developing starfish egg. Instead of separating the first two cells from each other and getting just two identical twins, the experimenter can wait until the four-cell stage is reached, separate these four cells, and get four embryos. He can also get eight complete embryos from the eight-cell stage. The separated cells of still later cell stages seldom or never develop into complete embryos. In other animals the process cannot go so far as in the starfish. In the frog, for example,

it is possible to get only two identical twins, from the first two cells. In still other animals the number may be just 4. The precise number that can be obtained is determined, possibly, by the stage at which differentiation sets in. If all the cells are still unmodified at a given cell stage, then each can still develop into a complete embryo. But if they have already got started along different paths in development, then the tendency is for them to continue along these paths, even when they are separated from the other cells; and they tend to develop into a part rather than into an entire new individual. As a rule an isolated group of cells does not complete its development into an isolated organ, but it may continue for some time in this direction, sufficiently so to show the experimenter that an isolated organ is being developed and not an entire new individual. The mass finally goes to pieces, probably because it does not receive the necessary support from other organs, and also because it is out of its "normal" environment, which is contact with other parts of the developing embryo.

In some species it does not seem possible to produce identical twins by the ordinary experimental procedure. If the first two cells are separated from each other, each tends to go right ahead and develop into its half of the body; or if the cells are separated at the 4-cell stage, they tend to develop into the particular part of the body that they would have, had they remained together. It is possible to explain cases of this sort by assuming that differentiation has set in at a very early stage, when the egg was yet undivided. The various parts of the egg became different possibly on

account of the formation of different kinds of materials in various regions of the egg. When cell division sets in, these regions become separated from each other by the cell boundaries and they pursue the particular path of the development to which they are predisposed by their included materials. Each cell accordingly develops into some particular organ or other part of the body, and tends to do so even after the cells have become separated from each other. It is, therefore, impossible to get identical twins from them.

Just what the various factors are that cause a cell to pursue one or another course in development is not definitely known. They are undoubtedly very numerous and complicated. Certain traits are dependent in development upon secretions produced by glands in other parts of the body. Thus the thyroid glands are necessary for normal development, and if they are defective or deranged, the individual develops into a cretin. Secretions from the reproductive organs influence the development of those traits which characterize the sexes and which are known as secondary sexual characters — the breasts and general form of the female, the voice and beard of the male, etc. Numerous other secretions could be mentioned that have a developmental influence. They are only some of the numerous possible factors that determine the precise path that the cells take in development. Contact is another factor, previously mentioned. Other factors possibly are accessibility to oxygen, food supply, temperature, amount of light, etc.

It is known for example that temperature speeds up the general rate of growth and development. But a

knowledge of this fact hardly helps in the solution of the problem before us. Here is the difficulty: the early embryo is a mass of cells which apparently are all alike. Are they really all alike? If so, then why do some develop into arms, others into legs, etc.? You say maybe they are different from each other. But then why is it possible to get identical twins from them by merely separating them from each other? This fact indicates that they are all alike in their hereditary constitution. The further fact that they are produced by mitotic cell division indicates the same thing. The problem before us is, How does it happen that in this uniform mass of cells, uniform in their developmental possibilities, some pursue one course, others another in the developing embryo and so give rise to different organs? If it could be discovered that conditions were not the same throughout this uniform mass of cells, or rather throughout this mass of cells which in themselves are uniform, then it is readily conceivable that a certain condition in one part of the cell mass might cause the cells here to pursue one course of development and a different condition in another part might cause the cells there to pursue quite another path.

A mere increase in temperature could not in itself cause one cell to do one thing and another cell identical in kind, quite another. If, however, the inside cells were of a higher temperature than those outside, due to their greater protection, then it is conceivable that those on the inside might be caused to develop differently from those on the outside. The localized region of the temperature would, in turn, be due not to any original difference in the cells, but would merely

come about automatically as the cells increased in number. Numerous other conditions might in similar manner make their appearance during the course of development and each might have a limited sphere of influence. In other words, it is possible that numerous localized conditions or differences automatically make their appearance in the growing cell mass, each condition having some specific influence on development and causing the various cells to pursue different paths in development, the cells themselves all being alike genetically, but pursuing different paths in development in accordance with the specific action of the localized conditions. One of the problems that confront the biologist is to find out what these localized influences are, and precisely what their action is on development.

As the cells start to become differentiated they naturally create further differences and these must be added to those which were present in the simple cell mass and which started the cells off along different directions in development. In this way, conditions in the different parts of the embryo become extremely varied. The reactions of the cells and their growth into organs become correspondingly varied.

The action of the glands on development must be explained in a slightly different manner. Their secretions are poured into the blood and reach all parts of the body. No one part receives more of the secretions than any other. Still some parts of the body show a decided effect of their influence, other parts not, as is especially evident in connection with the secondary sexual characters that develop under the influence of secretions coming from the reproductive organs. By the time

these glands begin to function, however, the individual has already got along pretty far in his development and the various cells of his body are differentiated. Now, it is conceivable that a given secretion or other influence might encourage the growth of some cells, but check the growth of others or have no influence on them at all, depending upon the type of cell. In general, once the cells have got started along different lines in development, then they are no longer necessarily responsive in the same manner to a given influence.

Why an animal or plant should replace just those parts that are lost by accident, and no others, and moreover why the wound should be the stimulus to renewed growth, are special problems in regeneration. Cut an earthworm into two and the missing tail end will be replaced in the one piece, and the head end [1] in the other, in both cases at the cut surface. If now, instead of simply cutting the animal into two, you should cut a piece out of the middle, you would find that the front end replaced a new head and the hind end a new tail. The piece might have been taken almost anywhere from the worm, so long as it was not too near either end; and in each case, the result would have been the same. Why is it that a given cut surface will always replace the head end if it happens to be at the front end of a cut piece, and a tail end if at the hind end? The result reminds you very much of what happens when you cut a magnetized piece of iron into pieces; in each piece, the end that was nearer the plus pole of the original magnet becomes plus, and the other end becomes minus. The

[1] The entire head end is not replaced if the portion removed exceeds a certain amount.

magnet is said to be "polarized," or to have "polarity" (because it has plus and minus poles), and each piece assumes this polarity after it is removed from the entire magnet. By analogy, the worm is said to have polarity (because its two ends are different), and its pieces are said to have, or to assume, polarity after they are cut out of the animal, each piece maintaining its polarity in the same direction as it was in the original worm; that is, having the power to develop a head at the front end and a tail at the hind end.

Polarity is shown by the cut out pieces of a great many of the lower animals and plants. Just what its cause is, has been a matter of speculation and experiment. It has been found in numerous cases that the head end of an animal is more active than the hind end; that is, more active in regard to the chemical changes that take place within its cells, as shown especially by their rate of oxygen consumption. There is supposed to be a gradual change in the oxidative rate as you go towards the hind end, such that at any particular level along the animal's length, the rate is higher than farther back, and lower than farther forward. One might visualize the process as having a slope or gradient like an inclined plane. The animal is, in fact, said to have a "gradient of oxidation"; or, to use a more general term, a "gradient of metabolism," a term which includes other chemical changes in addition to oxidation. The gradient is referred to as an "axial" gradient, because it runs along the long axis of the animal. When now, a piece is cut out of the length of the animal, the fore end would according to the theory always have a higher rate of metabolism than the hind end of the

piece, no matter from what level it was taken. The higher metabolic rate at the fore end is supposed to initiate head formation. Once the head starts forming there, it is supposed that it somehow prevents head formation anywhere else in the piece and that its presence either directly causes the formation of a tail at the hind end, or that a tail forms here because there is nothing else left for this end to do. This view of how polarity arises in the cut pieces is known as the "axial gradient theory."

Experiments on plants have led to another view of the possible cause of polarity. If you should cut a piece out of a willow stem and put it in a moist place, upper end up, you would notice after a while that shoots would sprout out at the upper end, and roots at the lower. The piece has polarity, you would find. But suppose now that you had turned the piece upside down, so that the actual upper end is now below. You would find that at first shoots would make a feeble start at the end that is now lower, and roots at the opposite end that is exposed to the air. But after a while shoots would grow at the exposed upper end and roots at the lower buried end. The original polarity has been "reversed" so to speak. Apparently gravity has something to do with the process. It has been thought that possibly there are substances in the plant some of which cause shoot formation and others root formation. If these were differently subject to the action of gravity, such that there were lighter substances that tended to go up and heavier ones that went down, it is conceivable that they might determine polarity, and that the direction of the polarity might be reversed if the direc-

tion of their flow were reversed when the piece is turned upside down. It might take a little while for this reversing action of gravity to take place and therefore the polarity of the piece would start in one direction and later be reversed. It is possible that there is just one substance instead of two, let us say one that starts shoot formation, subject to the action of gravity in such a way that it is forced towards the top of the stem; and that once shoots start forming under its influence in one place, roots have to form somewhere else.

In brief, the view just presented claims that polarity is due to organ-forming substances and is subject to the influence of gravitation. It is known as the "formative stuff" theory. Certain of the lower forms of animal life are like plants in that they are permanently attached to solid objects and branch, and the formative stuff theory can be applied to them; for the direction of their polarity is determined by gravity.

It is possible that both of the views above presented are true; that the axial gradient theory applies to the free living forms of life and that the formative stuff theory applies to the attached forms. Or, in fact, the two views may not be fundamentally different, in that the metabolic gradient which the one theory postulates may be dependent upon a gradient of materials which the other theory assumes.

Whether "axial gradients" and "formative stuffs" have any influence on early development, as well as on regeneration, is an undetermined question. If they have, they are simply two factors in addition to the numerous others that undoubtedly influence devel-

opment. Let us bear in mind that development is a highly complicated process subject to all sorts of factors. Contact, internal secretions, axial gradients and formative stuffs are only a few of the numerous possible things that influence it. All of these factors, whatever they are, merely condition development in the sense that they determine which of the numerous possible paths the cell will take in development. The various possibilities, however, reside within the cell itself and are dependent upon what is probably the most highly organized material in the universe, the substance that constitutes the chromosomes and in particular the genes within them, the ultimate units of heredity.

CHAPTER X

THE METHOD OF LOCATING THE ULTIMATE UNITS OF HEREDITY — LINKAGE AND CHROMOSOME MAPS

When biologists peered through their microscopes and saw chromosomes for the first time, little did they suspect that what they were looking at was the material basis of inheritance. There was nothing about the looks of a chromosome that gave any hint as to its importance — it was a rod-shaped body which took stains a little more readily than the rest of the cell. That, apparently, was all there was to it. The microscope, even its highest powers of magnification, did not make visible within a chromosome the finer structures which we now refer to as the genes. But the genes were there, and what was more, they had a definite arrangement: they were strung out in a single file like the beads in a string — in "linear" arrangement, so to speak. Even if the microscope had made visible the genes to the biologist, it would not necessarily have told him much about their nature. It would probably have shown him bodies that appeared simply as minute specks of protoplasm not strikingly different in superficial appearance from the protoplasm in other parts of the cell. Their real nature would still have been in the dark, and no amount of patient peering through a microscope could by itself have given the biologist a

hint as to what these bodies were for, even if he had seen them. To find out their real nature, he had to use a totally different line of attack, the method of the breeder.

It was through breeding experiments that Mendel discovered the units of heredity that we now refer to as the genes. He found that these units were separable from each other in the process of inheritance. But Mendel could not by his methods discover the chromosomes. The microscope was necessary for this. Much less could he tell us that the genes were in the chromosomes. It was only when breeder and microscopic worker got their heads together that each understood the other and, in fact, understood himself. Just what was it that they found in common, or rather, in parallel?

Mendel, in working with pea plants, noticed a peculiar thing about his units: they ran in pairs. We call the members of a pair "allelomorphs." The peculiar thing about allelomorphs was that they always separated from each other before the plant reproduced and they entered separate reproductive cells. Thus, when Mendel got hybrids by crossing a tall and a dwarf variety of peas, he found that the hybrids formed reproductive cells that contained either the tall unit or the dwarf unit. Or again when he crossed a wrinkled and a smooth variety, the reproductive cells of the hybrid contained either the smooth or the wrinkled unit. Never, so far as Mendel could see, did two members of the same pair of allelomorphs ever enter the same reproductive cell. The microscopic worker noticed the same sort of thing in connection with the chromosomes; they too ran in

pairs, and the members of a pair always separated from each other before they entered the reproductive cells.

Mendel further noticed that one pair of allelomorphs was not tied, so to speak, to any other pair. Tall separated from dwarf; smooth from wrinkled — these were allelomorphs. But tall could go with either smooth or wrinkled; so could dwarf. The allelomorphs, Mendel found, segregated independently of each other. The same sort of thing holds true of the chromosomes. In fact, if you put Mendel's allelomorphs in the chromosomes, they will do the very thing that Mendel found they did.

But if you examined the cells of Mendel's pea plants under the microscope and saw the chromosomes, you could not tell which one of them contained a particular gene. The chromosomes of a tall plant look exactly like those of a dwarf plant. A hybrid formed by crossing the two races contains the tall gene in one of its chromosomes and the dwarf gene in another. We know that the two chromosomes in question form a pair, but all of the chromosomes run in pairs and which of the several pairs happens to contain the tall-dwarf allelomorphs is something we cannot tell by mere inspection of the chromosomes.

In many animals, however, including man, there is a chromosome that has not an exact mate in the male — the X-chromosome — and it contains genes which, in certain cases, can be definitely identified with it. Take for example, the gene for color blindness in man (*c*) and its normal allelomorph, "not-colorblindness" (*C*). When a normal man (who carries *C*) mates with a color blind woman, he transmits to all of his daughters his normal

gene; he does not transmit it to his sons (see page 70, Fig. 25. This is precisely what happens to his X-chromosome; it also goes to all of his daughters but to none of his sons. Obviously, the gene *C* is associated with his X-chromosome, and presumably is contained in it. It is tied up with his X-chromosome in inheritance. To use technical language the gene in question is "sex-linked." Note, however, that the existence of the normal gene (*C*) in the X-chromosome would not have been known unless its abnormal allelomorph (*c*) also had been in existence. For if there were no people with the color blind gene (*c*), then all the offspring in any family would be normal and it would be impossible to say that certain offspring (the daughters) had received their normal gene from their father rather than from their mother. It is only when the mother is color blind and the father normal that this fact comes out.

The normal gene (*C*) undoubtedly gave rise to the color blind gene by mutation. Probably many other genes besides *C* exist in the X-chromosome of man, but in the absence of mutation, we cannot be made aware of the fact. There is, however, another defect in man which has the same "sex-linked" hereditary basis as color blindness. The defect in question, known as "hemophilia," is characterized by excessive bleeding from even slight wounds, and is due to a lack of clot-formation by the blood. The gene involved ("hemophilia," *h*) probably arose by mutation from a gene ("not-hemophilia," *H*) normally present in the X-chromosome.

If now, a man were both color blind and hemophilic, he would transmit to his daughters his X-chromosome

and both of the abnormal genes (*c* and *h*) that are contained in it. They would probably not show either trait, however, for their mother in all likelihood would be normal, and would transmit to them the normal genes *C* and *H* in her X-chromosome. Any daughter would be hybrid because she had *C* and *H* in one of her X-chromosomes, and the allelomorphs *c* and *h* in the other. She could be represented by the formula $\frac{C\,H}{c\,h}$. The genes occupy definite positions or "loci" in the chromosomes, and a female of composition $\frac{C\,H}{c\,h}$ could be referred to as hybrid at both the "*c*" and "*h*" loci.

What now would her children be like, especially her sons, who receive their one X-chromosome from her? Half would be color blind and half would be hemophilic. But would the half who were color blind also be hemophilic, and the other half normal? This question has not yet been definitely answered for man because there are no records of women who happen to be hybrid at both the *c* and *h* loci. But we have some evidence, got from a lower animal, which sheds light on the question.

In the insect Drosophila, a fairly large number of mutations have occurred in the X-chromosome and a correspondingly large number of sex-linked genes have become manifest. For example, a mutation changed the eye color of the animal from red to white. When a red-eyed male was crossed to a white-eyed female, all of the daughters were red-eyed, and all of the sons white-eyed.

This case is obviously similar to color blindness in

man. The white-eyed fly has in its X-chromosome a gene, white (*w*). The red-eyed fly has in place of this gene, the allelomorph "not-white" (*W*), dominant to white, and normally present in the X-chromosome. A red-eyed male transmits to all of his daughters his X-chromosome and with it, the dominant allelomorph "not-white" (*W*). The white-eyed mother transmits to her daughters one of her X-chromosomes together with the gene "white" (*w*). But the dominant allelomorph "not white" (*W*), that comes from the father, makes all of the daughters red-eyed. The sons, on the other hand, have only one X-chromosome. This they received from their mother, together with the gene for white-eyes; and for this reason, all of them are white-eyed.

It was not known that the mutation to white took place in the X-chromosome until after a cross was made. It then became evident that gene and chromosome went together in inheritance and that the one was presumably contained in the other.

Another mutation in the X-chromosome of Drosophila was one that caused the wings of the animal to become shorter and produced a race, called "miniature," that had the gene "miniature" (*m*) in place of the normal gene "not-miniature" (*M*). The new gene and its normal allelomorph were known to be in the X-chromosome because they showed the same "sex-linked" inheritance as the genes "white" and "not-white." It was, furthermore, found possible by hybridization to produce a race that had both white eyes and miniature wings, and that contained both the sex-linked genes "white" and "miniature" (called

"sex-linked" from the fact that they were in the X-chromosome).

A female could now be got containing in one of her X-chromosomes both "white" and "miniature," and in the other one, the two normal allelomorphs "not-white" and "not-miniature"; in symbols $\frac{wm}{WM}$. When she produced offspring her sons for the most part had either white eyes and short wings, or red eyes and long wings. This was to be expected, because her sons received just one of her two X-chromosomes. Some got the one that contained white and miniature (*wm*); others got the one that contained not-white and not-miniature (*WM*). But in addition to these sons, she produced some that had white eyes and long wings; others that had red eyes and short wings. Such sons were referred to as "cross-overs." About 30% of the sons were "cross-overs." They could be accounted for by assuming that the chromosomes exchanged parts somewhat as shown in Figs. 34 and 35. This process, referred to as "crossing-over" is supposed to take place just previous to the formation of the reproductive cells,

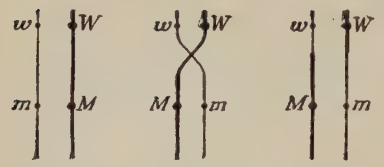

FIG. 34. Diagram to show crossing-over between *w* and *m*.

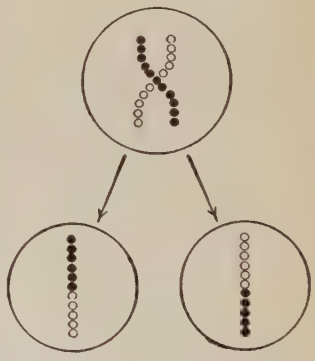

FIG. 35. Diagram to show crossing-over.

at the time that the reduction division takes place and the chromosomes come together in pairs. When crossing-over occurs between the white and miniature loci, we get recombinations between the genes (giving us *Wm* and *wM*). This happens in about 30% of the cases when the chromosomes pair. In the remaining 70%, there is no crossing-over between the chromosomes, and we get the genes in their old combinations (*wm* and *WM*).

Mendel, on the other hand, found that the recombinations between his allelomorphs, when he was dealing with two pairs, were as frequent as the old combinations, each forming 50% of the total (see Fig. 36). He referred to this fact by stating that the allelomorphs segregated independently of each other. One allelomorph was not tied to another belonging to a different pair. Presumably the allelomorphs with which Mendel dealt were in different pairs of chromosomes, and for this reason they showed independent segregation. But when two genes are in the same chromosome they are tied to each other and tend to go together to the offspring. They are said to be "linked."

Numerous other mutations took place in the X-chromosome of Drosophila in addition to white and miniature and in this way the genes at many loci in the X-chromosome became manifest. All such genes were found to be linked to each other. The amount of crossing-over between two loci was not necessarily the same as that between white and miniature (30%). It might be as little as 0.1%, but was never as much as 50%.

The actual amount of crossing-over could be accounted for on the assumption that it was determined

by the distance apart of the loci. In general, the greater their distance apart, the greater would be the percent of crossing-over between them. Crossing-over, it was assumed, might occur anywhere along the length of the

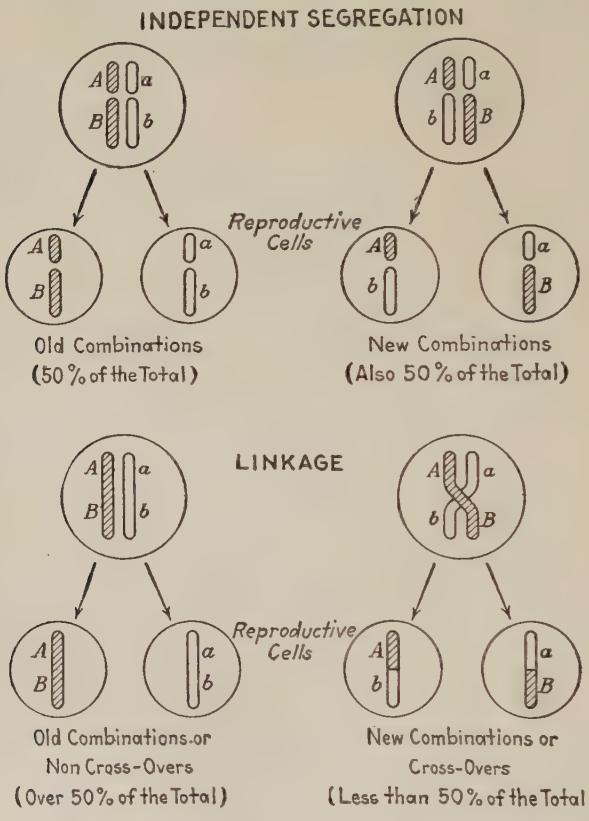

FIG. 36. Independent segregation and linkage compared.

chromosome, just where it took place being a matter of chance somewhat as might be expected of shots fired from a rifle at a line by a person who was not aiming at any particular spot on the line. More shots would

strike the line over a length of two feet than over a length of one foot — twice as many, on the average. So with the process of crossing-over. If two loci were separated say by the full length of the chromosome, there would be more chance of crossing-over occurring between them than if they were close together.

It is impossible to see the genes and to tell by direct measurement how far apart they are in a chromosome of Drosophila or in any other animal, but the amount of crossing-over serves as an index of their distance apart if the one (amount of crossing-over) is dependent upon the other (distance apart). Such an index does not tell us in actual fractions of an inch how far apart two loci are. It merely tells us that if there are say 2% of cross-overs between two loci, and 1% between two other loci, the first two are twice as far apart as the second two. When there is just one percent of crossing-over between two loci, the two are said to be a distance of one "unit" apart. Two percent of crossing-over means a distance of two units, ten percent, ten units, etc.

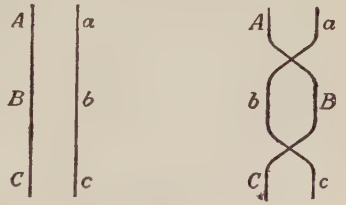

FIG. 37. Diagram to show double crossing-over.

Occasionally the chromosomes twist about each other twice, instead of just once (see Fig. 37). This is referred to as "double crossing-over." Suppose now that genes *A B C* were in one chromosome and *a b c* in the other. Then a double cross-over between *a* and *c* would not result in any recombination of the genes at these two loci. If we ignore the intermediate locus *b* we have *A C* in one chromosome, *a c* in the other;

and this is true after as well as before double crossing-over has taken place. Without the intermediate locus *b* we could not tell that anything had taken place between loci *a* and *c;* there is not evident any recombination of the genes, the thing that ordinarily shows us that crossing-over has taken place. If, therefore, we ignore the intermediate locus *b* and get the distance between *a* and *c* directly, we also ignore the double cross-overs and so the distance we get between *a* and *c* is shorter than if we took into account the intermediate locus *b* and the double cross-overs. Thus, if the two shorter distances *a* to *b* and *b* to *c* were 10 and 20 respectively, we would get 30 by adding them together. This would give us the total distance between *a* and *c*, as got by adding together the two shorter distances and taking into account the intermediate locus *b*. But if we got the distances between *a* and *c* directly, by simply getting the number of recombinations between the genes at these two loci, then we would overlook the double cross-overs, and instead of getting a distance of 30, we would get a somewhat shorter distance (about 28 it happens to be). In brief, the distance between two loci is greater if got by adding together the shorter intermediate distances, than if got directly.

When two genes are in the same chromosome we never get more than 50% of recombinations between them, regardless of how far apart they are in the chromosome. We could, accordingly, never get a distance that exceeded 50, if we got our distances directly, by simply getting the proportion of recombinations between the genes. But if we add together the shorter distances, we may get a figure that exceeds 50 for the distance be-

tween two genes. For then we take into account the double cross-overs and add them to the singles in making up our total distance. A double cross-over between *a* and *c* may be regarded as made up of two singles, one between *a* and *b*, and another between *b* and *c*. When the total distance is got between *a* and *c*, a double cross-over counts as much as two singles.

Experiments especially designed for the purpose are necessary in order to get accurately the proportion of double cross-overs between two loci, *a* and *c* let us call them. But if we know the proportion of single cross-overs between *a* and *b*, and between *b* and *c*, we can estimate roughly the proportion of doubles that we ought to get between *a* and *c*. Possibly an analogy will help to see how we can get at such a figure. Suppose you knew that 10 percent of the people in a certain place were tubercular and 20 percent had blue eyes, and that you knew further that blue eyes had no connection with being tubercular. Then what percent of the people in this town would you expect to be both tubercular and blue-eyed? Obviously, 10% of 20, or 2%. Just so with crossing-over. If there is 10% of crossing-over between *a* and *b*, and 20 between *b* and *c*, then there should be 10% of 20, or 2% of double crossing-over between *a* and *c*. That is to say, two single cross-overs would happen to come together at the same time in this proportion of cases, just as tuberculosis and blue eyes do, providing the one had nothing to do with the other and their coming together was just a matter of accident, a coincident, so to speak.

When experiments are run to test the proportion of double cross-overs, the "expected" proportion is some-

times got, sometimes not. The figure that is got depends on the distances involved. When the distances between the loci are small, one cross-over interferes with another one, just as in twisting two ropes about each other a twist at one point might interfere with another twist nearby. But when the distances are of a certain length, then there is no "interference" of one cross-over with another. The "expected" proportion of double cross-overs is realized; that is to say the proportion that is expected if two single cross-overs happen to come together as a coincidence as often as expected. Thus, if one distance (between loci *a* and *b*) were 10 and the other (between *b* and *c*) were 20, then the proportion of double cross-overs might be about what is expected (10% of 20, or 2%). In this case, we would say that the "coincidence" was 100%. But if we had got only 1% of double cross-overs instead of 2, that is half the "expected" proportion, then the "coincidence" would be 50% instead of 100.

The double cross-overs do not amount to much over short distances. But over long distances, they become more numerous and have to be considered. If it were not for them, the distance between two genes could never exceed 50 units in length. This follows from the fact that the proportion of recombinations never exceeds 50% when we are dealing with genes in the same chromosome. But when genes are widely separated and the double cross-overs added in with the singles, distances may be obtained that are 100 units or more in length.

Much of the earlier linkage work on Drosophila was done in connection with the X-chromosome and sex-linked mutations. But in addition to the mutations

that were sex-linked, numerous others occurred in Drosophila that were not sex-linked. The mutated genes and their normal allelomorphs showed no tendency to follow the X-chromosome; neither were they linked to any of the genes in the X-chromosome. It was evident from this that these non-sex-linked genes were not in the X-chromosome. As these mutations kept piling up and their relationships to each other were studied through crossing experiments, it was found that some were linked to each other, others were not. In general, the non-sex-linked genes fell into three groups, each group being made up of those genes that were linked to each other. Any member of one group was linked to all others in its group, but it segregated independently of those belonging to members of any other group.

Counting the group of sex-linked genes, there were in all four groups of linked genes. Corresponding to this fact, it was found that there were four pairs of chromosomes in Drosophila. Three of the chromosome pairs in Drosophila are large, and one pair is small. Corresponding to this fact, three of the linked groups contained each a comparatively large number of mutations and the fourth a small number. In short, there was a correspondence between the size of the chromosomes and the size of the linkage groups. It seemed reasonable to conclude that the genes were in the chromosomes and that they owed their linkage to this very fact.

The linkage relationships of the genes indicated that the genes had a definite arrangement in the chromosome. Consider first an analogy. If you were told that three points *a*, *b*, and *c*, were on a straight line and that *a*

and *b* were 10 inches apart, and that *b* and *c* were 6 inches apart, then *a* and *c* should be either 16 inches apart or 4 (according to whether *c* is to the right or to the left of *b*, see Fig. 38). This sort of relationship was found to hold for linked genes. The distance between two genes *a* and *c* (distance as indicated by percent of crossing-over) was found to be approximately either the sum or the difference of the distances between *a* and *b*, and *b* and *c*. Such a relationship indicated that the genes were arranged in a line in the chromosomes — that they had a linear arrangement.

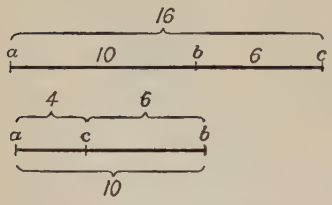

Fig. 38. Diagram to show the two possible arrangements of three genes, if the genes are in line.

It was found possible to get the relative positions of the genes in the chromosomes by means of their linkage relationships and to make what was known as chromosome "maps." The genes were plotted as points on a

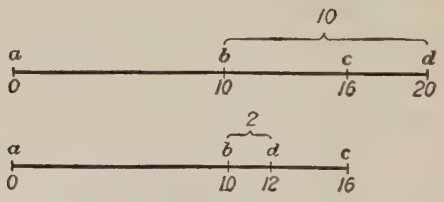

Fig. 39. Diagram to illustrate the method of placing any gene *d*, on a chromosome map.

line and were separated by distances proportional to the amount of crossing-over between them. To get the position of any gene on the map, it was necessary to get the amount of crossing-over between it and two other genes already plotted. Suppose, for example, that

genes *a*, *b*, and *c* were at points 0, 10 and 16 on the chromosome map and that we wanted to place gene *d* on this map (see Fig. 39). If we found that there was say 4% of crossing-over between *c* and *d*, this would mean that *d* was four units from *c* (which is at 16) and that it was either at point 20 or at point 12, depending upon whether it was to the right or the left of *c*. By finding the distance between *b* (which is at point 10) and *d*, we could decide which was the case. If this distance were 10, then *d* would be at point 20, four units to the right of *c* (see Fig. 39, *a*). If the distance were 2, then *d* would be at point 12, four units to the left of *c* (see Fig. 39, *b*). Once the new gene was placed on the map, say at 20, then it would be known what its distance was from all other genes on the map. Thus its distance from *a* is 20, from some other gene, say at 35, its distance is 15, etc.

From a knowledge of the distance between two genes on a Drosophila chromosome map, it was possible to tell how strongly linked any two genes were and how frequently they would both go together to the offspring even though no experiment had previously been made to determine this point directly. Chromosome maps, in brief, gave very valuable information in Drosophila regarding the probable genetic composition of the offspring.

A knowledge of chromosome maps will undoubtedly prove of similar great value to the human race, once chromosome maps are made for it. Take a simple example. Suppose a woman had a color blind father, and in consequence were hybrid for color vision $\left(\frac{c}{C}\right)$. We know that some of her sons are going to be color blind

(those that get *c*), and others normal (those that get *C*). But we would not know at the time her children were born which of them had the defect and which did not. Suppose now she had in the chromosome that contained *c*, and close to *c*, some other gene *A*, for some physical trait that appeared at the time of birth, or soon after; and in the chromosome that contained *C*, she had the gene *a*, allelomorphic to *A*, (so that her genetic formula was $\frac{Ac}{aC}$). Then as a rule the children who got *A* would get *c*, and those who got *a* would get *C*. It would thus be possible, by looking for the physical trait in question to tell whether or not a child was going to develop color blindness. His training in matters that involved color discrimination could be shaped accordingly. It will be seen that the gene for the physical trait serves as a "label," so to speak, for the color blind gene (or its allelomorph).

More important than the matter of color blindness would be the mentality of the child. There might be certain genes that are necessary for the development of special talents. It would be very desirable to know at an early stage in development whether a child possessed such a gene. A chromosome map would be of great assistance in this connection; for it would supply us with "labels" in the form of other genes that were linked to the one for the mental trait and that expressed themselves early in development in the form of easily recognizable physical traits.

Chromosome maps would be of assistance in another way. A special talent might very well be dependent not upon just one gene, but upon several; and the genes

in question might be scattered over several chromosomes. If a man had all of the genes for the talent in question and if he were not hybrid then he would transmit all these genes to every one of his children. But if he were hybrid, then only some of his children would get all of them. To know whether or not a child had received all of these genes from either or both parents it would be necessary to have maps of all the chromosomes in which such genes were located, in order to have the other necessary identifying genes that act as "labels."

At present, we have no chromosome maps at all for man. Their construction will involve a tremendous amount of labor and careful study. Consider for a moment how they were got for the insect Drosophila. The gene "miniature" (for short wings) was found to be located about 30 units for the gene from white eyes. But before this could be discovered, it was necessary first to get flies hybrid at both the white locus and the miniature locus, then to find out from the count of the offspring of the hybrids what percent of crossing-over there was between white and miniature.

This in itself was a rather tedious process. For the hybrids themselves did not occur in nature. They had to be made up by breeding together the white race with the miniature. It was from these flies or rather their offspring that the distance was got between white and miniature. Bear in mind that there was no way of telling from the looks of a white-eyed or a miniature fly that the genes white and miniature were in the same chromosome. Not even the hybrids could give us this information directly. It was only from the offspring of the hybrids that we could get it. The offspring had to

be classified and counted, in order to see what proportion were cross-overs. From this it could be inferred how much crossing-over took place when the reproductive cells were formed from which the offspring were derived, and so the distance between the two loci was arrived at. But now we have only two points on the chromosome map. For every other locus a similar procedure was necessary of getting hybrids and making large counts of their offspring.

In getting human chromosome maps, it would obviously be impossible to make hybrids to order. We should have to depend upon finding them by accident. The right kind of hybrid would be very rare. Consider, for example, the difficulty one would have in finding a woman who was hybrid for both color blindness and hemophilia, and then not only of getting one such person, but of finding a large enough number to get a thousand or so offspring from. Such numbers would be necessary to get a reliable estimate of what proportion of the offspring were cross-overs. Now we happen to know that the genes for color blindness and hemophilia are both in the X-chromosome, but by far the vast majority of other genes are in other chromosomes. Which of these are in the same, and which in different chromosomes is a matter which we do not know, so that we have even less information about them than about the ones that we have found in the X-chromosome. Moreover, any two genes taken at random would be much more likely to be in different chromosomes, than in the same one, for the same reason that two persons living in the same street and selected at random would as a matter of chance be more likely to be living in

different houses than in the same house, provided the number of houses in the street was fairly large, say 24, the number of chromosome pairs in man.

The difficulty therefore would be rather great of finding parents who happen to be hybrid at two or more loci in the same chromosome pair and of getting a sufficiently large number of their offspring to determine the amount of crossing-over between the loci. All of this will have to be done before human chromosome maps can be constructed, and only then will we be able effectively to study our hereditary make-up. But though the task is a difficult one, it is possibly one of the most important that confronts the human race, for it is only through a knowledge of our inheritance that we can predict and control it and assist the human race in its climb to a higher type.

The discoveries that were made in connection with Drosophila were of such an astonishing nature that many biologists for a while hesitated to believe them. In particular, they were not prepared to accept the conclusion that the units of heredity — the genes — were contained in the chromosomes. An analogy may help, possibly, to clarify the situation in regard to the chromosomes. If you should see a number of ships moving about in a harbor in the daytime, and at night not the ships themselves, but groups of lights moving about in a corresponding way, you would be justified in concluding that the lights come from lamps carried by the ships. The student of heredity is very much in this same position. He is dealing with genes that are arranged in a line in the chromosomes. The genes themselves are very small; they are concealed from his

direct view, just like the lamps within the ships in the daytime. But the chromosomes he can see and he can watch their movements, their transmission from one cell to another and from parent to offspring. Furthermore, he can see the effects of mutations. These correspond to the lights coming from the lamps. He can see that the mutated genes, like the lighted lamps, move in groups and that the groups correspond to the chromosomes. He feels justified therefore, in regarding the genes, both the mutated and the unmutated, as being lodged in the chromosomes.[1]

This conclusion, if true, must be ranked with the important discoveries in physics that had such momentous applications in the last two or three decades. It is conceivable that the biological discoveries may prove even more momentous should they be applied to the improvement of the human race.

[1] H. J. Muller suggested this "ships in harbor" analogy.

CHAPTER XI

THE NEGRO-WHITE CROSS AND THE MORE COMPLICATED FORMS OF INHERITANCE: MULTIPLE FACTORS

When the white and black races came into contact in America, there took place an experiment in racial intermixture which at first seemed in no way connected with Mendel's hybridization experiments on peas. The blacks and whites crossed and produced a mixture which truly seemed like a mixing of bloods. From it neither race again emerged in its pure form, regardless of the number of generations that elapsed since the hybrids were first produced.

Not so with the experiments of Mendel. He was able to extract from his crosses, apparently unmodified, the races which entered the cross. The hybrids which he produced in the first generation were indeed hybrids, a mixture of two races; but they gave rise in the second generation to offspring which in every detail resembled their pure grandparents, some reverting to the one race, others to the other race. What is more, they continued true to type in the offspring they produced in later generations. There were, to be sure, some hybrids in the second generation, in addition to the pure types, but they too were capable of producing pures and were in no way different from the hybrids of the first generation.

Mendel explained his results by assuming that each

parent race had some hereditary unit characteristic of it (let us label the units *A* and *a*). When the races were crossed, the units of each race came together in the hybrid $\left(\frac{a}{A}\right)$, but did not mix with each other. Moreover, before the hybrids reproduced, the units entered separate reproductive cells and thus made it possible for the hybrids to have offspring of the pure types. For whenever two reproductive cells met having units of the same type (either *A* or *a*), they produced offspring of pure type $\left(\frac{A}{A}\right)$ or $\left(\frac{a}{a}\right)$.

We now refer to Mendel's units by a definite term, the genes. They are the ultimate units of heredity in the sense that they do not break up into still finer particles as we follow them from generation to generation, nor do they lose their identity by mixture with each other. Each race that Mendel worked with contained not merely one kind of gene, but many, possibly thousands. One of these was different in each race from one in the other race with which it was crossed, but all the other kinds of genes with which the observer was concerned (*B*, *C*, *D*, etc.) were the same in the two races. There was, in other words, only one genic difference noticed between the races that Mendel crossed.

But between the human races, there are many conspicuous genic differences. If we confine ourselves to just the genes that influence the amount of blackness in the skin in the negro and white man, then, according to some recent studies[1] there are two kinds of genes

[1] Made by C. B. Davenport, of The Station For Experimental Evolution, New York.

characteristic of each race, *A* and *B* of the negro, *a* and *b* of the white man. There are additional genic differences that influence skin color, but they have a minor effect and we shall omit them from our consideration. There are also probably many genes for skin color which the negro and white man have in common, but it is not necessary to take them into account.

When the negro and white races cross, they produce a hybrid, the mulatto, who receives from his black parent the genes *A* and *B*, and from his white parent the genes *a* and *b*. Accordingly, the mulatto is of composition $\frac{A}{a}\,\frac{B}{b}$. It is true now that the mulattoes produce offspring who are intermediate in color like the mulattoes themselves, and who show little or no tendency to revert to the original pure racial types. But occasionally in a mulatto family there is a child who is much lighter than the rest. He has, to be sure, many of the characteristics of the negro, or rather of a mixture of the races, and would not often be confused with a pure white child. But so far as his skin color is concerned, he is practically as light as a white person. This is true even when there has been no further breeding with the white race, but only the interbreeding of mulattoes of the first generation, having the genic composition $\frac{A}{a}\,\frac{B}{b}$. Occasionally too, a very dark child is produced, almost as black as the pure negro.

Now, the reappearance of the pure types, or rather of the extreme color types, would not be expected even occasionally if the two races had become permanently and irrevocably mixed in the sense that their character-

istic genes had lost their identity through mutual contamination. For otherwise the intermediate type would persist, like wine and water that had once been mixed, never to become separated again from each other. But if the genes themselves did not mix and each preserved its identity, then, and only then could the mulattoes produce offspring of the extreme types. For the individual genes would leave the mulatto in the same pure form as they entered him. Before they leave him to pass on to the next generation, they enter his reproductive cells. This they do in various possible combinations, making reproductive cells of different types, some of which contain only the negro genes *A* and *B*, others only the white genes, *a* and *b*. When mulattoes mate, the reproductive cells come together in fertilization, one from each parent in the production of a child; and should each reproductive cell happen to contain the white genes *a* and *b*, then there would result a fertilized egg containing nothing but white genes $\left(\frac{a}{a}\,\frac{b}{b}\right)$, and this would develop into a child that is almost pure white in color. On the other hand, had each of the reproductive cells that met contained just the black genes *A* and *B*, then the offspring would have been of the other extreme type $\left(\frac{A}{A}\,\frac{B}{B}\right)$, practically pure black.

There are other types of offspring possible in addition to the two just mentioned; namely, the intermediates that connect the two extremes, and these in fact outnumber the pure types. But the intermediates also would be expected to make their appearance, even if

there had been no mixing whatever of the genes. For not only might two reproductive cells of similar type meet and produce the pure types, but one with the negro genes *A B* might combine with one having the white genes *a b*, producing a child of composition $\frac{A}{a}\frac{B}{b}$, exactly like the mulatto parents and again intermediate in appearance.

The combinations considered so far do not by any means exhaust all the possibilities. For the genes enter the reproductive cells not only in the two combinations already mentioned, *A B* and *a b;* but also in two others, *A b* and *a B*, giving in all four types of reproductive cells (*A B*, *a b*, *A b*, and *a B*). These are all produced in a mulatto, and in about equal proportions; and there is nothing to prevent them from coming together in all combinations theoretically possible when they meet in the production of the offspring. There is just one thing that the genes must do, and that is obey Mendel's Law. They are partners in the hybrid, but they do not mix with each other. And further, those that are partners (the allelomorphs of Mendel) again separate before the hybrid reproduces, *A* from *a*, and *B* from *b*, and enter different reproductive cells. Whether *A* "chooses" to go with *B* or *b*, makes no difference, so long as it goes with either; and *a* is given a similar choice. The result is reproductive cells of the four types: *A B*, *A b*, *a B*, and *a b*. These are all produced by any mulatto.

The pure black parent has reproductive cells of only one type, *A B;* and when he mates with another black he can produce offspring of only one type $\left(\frac{A}{A}\frac{B}{B}\right)$.

Pure whites, when interbreeding, also produce offspring of only one type $\left(\frac{a\,b}{a\,b}\right)$, since the genes *a b* come from each parent. The mulatto, on the other hand, has a variety of reproductive cells and when he mates he can have a variety of offspring.

Consider, for the sake of simplicity, what would happen if the mulatto mated not with another mulatto, who also produces four types of reproductive cells, but with a pure negress, who produces just one type, *A B*. In this case, any child would receive from its mother the genes *A B*, because all of her eggs agree in containing *A B* and can transmit no others to her offspring. But from his father, the child might receive any one of four combinations: *A B*, *A b*, *a B* or *a b;* for the father produces sperm cells of all four types. Suppose for example, that a sperm cell of the second type (*A b*) should fertilize an egg. Then the child would receive from his father the genes *A b*, and from his mother her only possible combination *A B*, making him of genic composition $\frac{A\,b}{A\,B}$; genes shown above the lines (*A b*), coming from the father, those below (*A B*), from the mother.

But any of the four types of sperm cells, not just the one mentioned, might fertilize an egg, giving four possible types of offspring: $\frac{A\,B}{A\,B}$, $\frac{A\,b}{A\,B}$, $\frac{a\,B}{A\,B}$, $\frac{a\,b}{A\,B}$ (where again, the genes coming from the father are shown in each case above the lines, those from the mother below). This is the case when one parent, the mother, is pure and produces only one type of reproductive cell. But should she also be a mulatto, then she, like her husband, would

produce four types of reproductive cells, each of which could enter into four combinations with the sperm cells, making possible a total of 4 × 4, or 16 combinations. These combinations could readily be arrived at by considering each type of egg separately and allowing it to be fertilized by the four types of sperm cells (see Fig. 40).

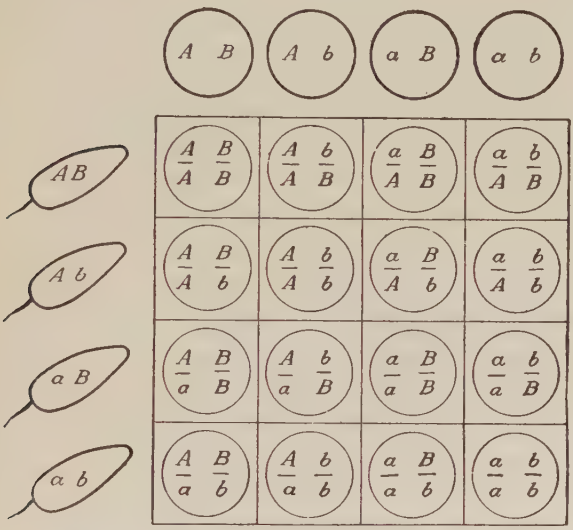

FIG. 40. Diagram to show the combinations between the reproductive cells of mulattoes.

If you should go to the bother to examine and compare the formulas for these combinations, you would find that some of them were repetitions and that there were not 16 different types of offspring. But there would be a type with nothing but black genes $\frac{AB}{AB}$, another type with nothing but white genes $\frac{ab}{ab}$. These

would be the extremes of black and white. In addition, there would be offspring who contained genes of both kinds. Some would have two black genes and two white. They would be of intermediate shade, like their mulatto parents. Others would have three black genes and one white. They, too, would be somewhat intermediate in color, but would lean towards the pure dark type. There would also be some that had just one black gene and three white, and they would lean towards the pure white type. In general, the shade of darkness would, on the average, be determined by the number of black or white genes that a child had.

Note that a child always has four color genes. If he is intermediate and has just two black, the other two must be white. It is impossible to say whether he is intermediate because he has only two black genes, or whether because he has just two whites. The same thing is true of the other classes. They may owe their particular shade of color either to the number of black genes they have or to the number of white. But which happens to be the case makes very little difference so far as the result goes. The particular shade of darkness is determined on the average by the number of genes the offspring have of one kind or the other. If we limit ourselves to the black genes, we find the offspring fall into five groups; namely, those that have four black genes, those that have three, two, one and none. The offspring vary accordingly in darkness.

We should expect to find children of all these types in a family of mulatto parentage, provided the family was sufficiently large to allow for the appearance of all types. But the extreme types appear only in comparatively

small proportions, in one out of every sixteen offspring on the average; and in a small family they would as a rule fail to show up. On the other hand, the children of strictly intermediate type, those with two black genes, are the most numerous as a class, six out of every 16 offspring on the average. They would often be present in a family to the exclusion of the other classes. The next most numerous classes would be those which were

Number of Black Genes	0	1	2	3	4
Relative Number of Children	1	4	6	4	1

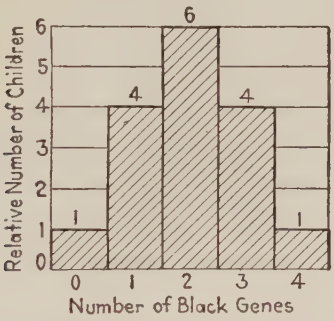

FIG. 41. Distribution of the children produced by mulattoes, according to Mendelian classes. The lower figure is a graphic representation of the data shown in the upper figure.

next darker or next lighter than the strictly intermediate class with two black genes, and which had either 3 black genes or 1. Each of these two classes would form 4 out of every 16 offspring on the average. Finally, there would be the extreme classes, which had either 4 black genes or none at all, and which would each show up in only 1 out of every 16 offspring on the average. These facts are shown in diagrammatic form in Fig. 41.

If you were actually to examine the children in mulatto families, you would find it practically impossible to put them into any definite classes and to count the number in each class. You would find that the darkest offspring were connected with the lightest by all possible intermediate shades. If the intermediates were lacking, you could easily make a classification and a count; for there would be just two classes, the darks and the lights, and when you examined any child you could without hesitation put him into the one class or the other. There would be, so to speak, a distinct "gap" in color which would separate the two classes from each other and make their classification easy. But suppose there were intermediates in addition. Then you would hardly know what to do with them. Not only this, but the extreme classes themselves would cease to exist as definite classes; for there would be no longer any gaps separating them from the intermediates. If indeed all the offspring with a given number of genes had a definite color, then there would be definite gaps separating the offspring with different numbers of black genes; and it would be possible to find that they fell in the definite ratio previously mentioned (1 : 4 : 6 : 4 : 1). But to be able to throw the offspring into any sort of a ratio, you must first be able to classify and count them. This is not so easy with the offspring of mulattoes. For offspring with a given number of black genes are not all of exactly the same color. Some are darker than others because of differences in the amount of sunlight to which they were exposed, and the darker offspring of one class sometimes connect up with the lighter of the next. Thus the gaps between the genic classes are in large measure elim-

inated. But by the use of a special apparatus, it was found possible[1] to detect differences in the amount of blackness that were rather small, and that would escape ordinary observation. The worker who used this apparatus measured and compared the amount of blackness in the offspring of first generation mulattoes, and he was able to discover several "gaps" in the amount of their skin color or rather, shades which individuals less often had, and so to place most of the subjects in several genetic classes.

There are, however, no definite Mendelian classes apparent to the ordinary observer in a mulatto family. But instead, there seems to be just one intermediate type which is subject to more or less variation in amount of darkness. This impression is exaggerated by the fact that the offspring who are strictly intermediate or almost so, are the most abundant. They, moreover, are the very offspring who would lead you to believe that the races had become permanently mixed and that the negro-white cross did not conform to the Mendelian interpretation. But closer analysis shows that the cross really conforms to the same simple principles as Mendel discovered in his races of peas. The genes of the black and white races do not permanently mix with each other in the mulatto. If they did, the extreme types would not show up again in the second generation, not even in small proportions.

The comparative infrequency with which the mulattoes produce the extreme classes as well as the abundance of the intermediate types is exactly what is to be expected on mathematical grounds. For when there

[1] By C. B. Davenport.

are two genic differences between the parent races instead of just one, then the hybrid becomes more complicated and produces reproductive cells in greater variety than when there is just the one genic difference with which Mendel dealt in his simple crosses. With increased variety of reproductive cells there is an increase in the number combinations into which the reproductive cells can enter with each other, with the result that they produce Mendelian classes of offspring in greater variety. The particular combinations that produce the extreme types occur rather infrequently compared with those that produce the intermediate types and so the intermediate offspring predominate. But the fact remains that the extreme types do make their appearance in the second generation.

In the first generation, however, the generation that consists of the mulattoes, no such extreme types ever show up. The reason is perfectly evident. The mulattoes are all of one genetic type. No matter how many of them are produced, they can never receive anything but *A B* from their black parent and *a b* from their white parent; and they must all be of the one genetic type $\frac{A}{a}\frac{B}{b}$, a type that appears strictly intermediate. But in the second generation there is a greater variety of genetic types, due to the production of the various Mendelian classes. There is a correspondingly greater range in color variation shown by the offspring. In the first generation, whatever variation there is in color is not caused by differences in the major genes that differentiate skin color. It is due entirely to differences in the amount of sunlight to which the mulattoes

are exposed; that is, to environmental differences, and to minor genetic differences in skin color, such as would distinguish blonds from brunettes in a wholly white population. Thus the mulattoes all belong to one and the same genetic class in regard to the genes *A*, *a*, *B*, and *b*, with which we are concerned. In the second generation, there also is some variation caused by the environment and minor gene differences, but in addition there is the genetic variation due to Mendelian recombination of the major genes concerned. For this reason, the range of variation is considerably greater in the second than in the first generation.

It is true that the mulattoes look intermediate as do also most of their offspring and they suggest that the inheritance of the pure races has become "blended" in them. The negro-white cross, in fact, has sometimes been referred to as a case of "blended inheritance," in contrast to "Mendelian inheritance." But if the genes had simply come together in a melting pot in the mulatto and formed a permanent mixture, a blend, then the mulattoes could do nothing but transmit to their offspring the mixture just as it was in them. So the second generation would all have to conform to the same genetic type as the first and the one could not possibly show any greater range of variation than the other. But there is increased range of variation in the second generation. This means that there has been an increase in the number of genetic classes, which increase in turn implies Mendelian segregation and recombination. In brief, increased range of variation in the second generation points unequivocally to just one thing: Mendelian inheritance.

The fact that the mulatto is intermediate in appearance does not necessarily imply that his genes have also become intermediate. His color is one thing, his genes quite another. The one, his color, makes its appearance in the course of development and is the expression of the other, his genes. There are genes of two kinds in the mulatto. Possibly each kind expresses itself and so causes the development of a color intermediate between that of the pure races. But each kind of gene remains separate and distinct in him and is transmitted unchanged to the next generation. This, in essence, is Mendelian inheritance.

To be sure, the two races never again emerge in their pure form after once they have mixed. The offspring of the mulattoes are never pure negroes or pure Caucasians, not even the exceptional extremes. They all show evidence of a mixed origin, even though their *color* may in some instances be almost that of the pure races. But bear in mind that skin color is not the only trait that is distinctive in the two races. There are the differences in the shape of their skulls, character of their hair, thickness of lips, and in numerous other traits. Even if every one of these traits when considered separately appeared again in its pure form among the offspring of the mulattoes, it would be extremely unlikely that one particular child should have in pure form all of the traits characteristic of the one race or the other. He might have the pure skin color of one of the races, say the white, but not the typical head form. It would be rather unusual for one and the same child to have both the skin color and head form of either race in pure form. And if a child did happen to have two pure traits,

he would be just as likely to have the skin color of the one race and the head form of the other, as to have them both of the same race, provided the two traits were due to separate genes. When all the other traits are considered in addition, it would be extremely unusual if all those of the one race should happen to come together into one child. He would be much more likely to have some traits of the one race, others of the other. This would be true even if each trait, when considered separately, made its appearance in pure form in a comparatively large proportion of the offspring, as was true of the traits with which Mendel worked in his peas. But probably most of the traits distinctive of the two human races are not separated by just the single genetic differences with which Mendel worked, but by two or more, as is true of skin color. In this event, it would be rather unusual for any given child to have any one trait in the pure form characteristic of the one race; and for him to have all other traits of that race, also in pure form, would be a virtual impossibility.

Theoretically it could occur, because all of the genes in the mulatto obey Mendel's law, regardless of what trait they influence and of how many of them there are that influence it. The genes that act as partners in the hybrid, the allelomorphs, in no instance mix with each other; they remain characteristically negro or white and again enter separate reproductive cells before they pass on to the next generation. But that all the negro genes should go exclusively to any one reproductive cell and all white to any other, is unlikely to the highest degree. The chances of receiving these two particular combinations would be slimmer than getting two decks of

cards again after thoroughly shuffling them and dealing them out to two persons at random. If you took out just two cards from each deck and shuffled them, you would fairly often deal to the two persons the same two cards that you removed from each deck; but as you increased the number from each deck to 3, 4, 5, etc., your chances of recovering the original combinations, after shuffling, would become less and less, and when the number included all cards in the two decks, a lifetime of continuous dealing would not suffice to recover each deck entire.

Just so when racial intermixture takes place. The genes become shuffled and it becomes practically impossible to recover again the particular combinations that constitute the original pure races. Theoretically, it might occur. But countless millions of offspring would have to come into existence before chance produced the rare combination necessary.

All the while, Mendel's simple principle would be in operation. The individual genes characteristic of each race would still be in existence, but only in combinations that are different from those of each pure race. The traits of the races have become mixed, but the genes are as pure as ever. Mendel's law applies to genes, the ultimate units of heredity; not to traits, the expression of the genes. It is the genes that are transmitted from one generation to the next, not traits. Once the fertilized egg has received certain genes, then it develops and the traits make their appearance as an expression of the genes. When the genes differ, the traits differ.

It so happened that Mendel crossed races between which there was just one noticeable genic difference affecting a given trait, and the offspring of the hybrids

developed one trait or the other in accordance with the type of gene that they received. But where there are several genic differences between two races, then the difference in the trait as it appears in the one pure race or the other is not determined by just one type of gene, but by two or more — "multiple factors," as they sometimes are called.

In the offspring of the hybrids, there are intermediate possibilities in the expression of the trait, in accordance with the number of genes they receive of one type or the other. The trait need therefore not appear in just one of two alternative forms such as pure black or pure white. Nevertheless the individual genes are transmitted by the hybrid in the same way as when the traits themselves appear in just one alternative form or the other. In either case, the genes have been transmitted in their pure form to the next generation.

It would be incorrect to state that there were two forms of inheritance, "blended" as contrasted to "alternative." Basically all inheritance conforms to one and the same principle, the principle observed by Mendel. It is only upon superficial inspection that the more complicated cases seem to conform to some other mode of inheritance.

The negro-white cross is by no means the most involved case of inheritance that confronts the student of heredity. Breeders have got hybrids by crossing animals or plants that belong to different species, and not merely to different races of the same species, as is true of the human races. The mule is a familiar example of a species hybrid. Mules are sterile and cannot reproduce, but if they could and were mated to each other, the

chances are that practically none of the offspring would belong to either pure parent species, the horse or the donkey. They would probably not have even one of the distinctive traits of either pure parent, let alone all. Instead, they would probably be intermediate in almost all respects — mules — not only in the next generation, but for all generations to come. It would appear much as though the hybrid formed by the cross had become a constant and fixed type.

In a case of this sort, the product of the cross is an extremely complicated hybrid, much more so than the mulatto. For the parents of the mule do not belong to the same species and they are not so much alike as are the races of man, in their hereditary make-up. The genetic differences that separate them are very numerous, not only as applied to the two species as a whole, but also to their individual traits. The difference in size of the two species, in their color, in the length of ears, or in almost any other trait is caused probably by many genic differences, and not just by two as was the case with skin color in man. It would therefore be extremely difficult to recover any one of these traits in pure form from the hybrids, even if they could reproduce. The situation is even more complicated than the negro-white cross. The offspring of mulattoes never have the same combination of traits as either pure parent race, though they may occasionally have an isolated trait of one pure race or the other, such as black or white skin. But the offspring of mules would probably never even show an occasional trait in pure form, or only rarely so. Practically every trait in the two parent species would be separated by wide genetic

differences and when the species mixed, it would be difficult to recover any trait in pure form.

Consider for a moment the difficulty of recovering the pure traits and see why the difficulty becomes greater with increasing number of genic differences. When there are just 2 genic differences that affect a trait, as skin color in man, then the trait appears on the average in pure form in one out of every 16 offspring produced by the hybrids. But when there are 3 genic differences, the pure traits, it so works out, appear in only one out of every 64 offspring. It will be seen that the frequency with which the pure trait makes its appearance goes down out of all proportion to the increase in genic differences. The reason for this is that the genes from each pure parent become shuffled about in the hybrid and enter his reproductive cells in various combinations which become greater in number with increase in the genic differences. When 2 different kinds of genes come from each pure parent (as *A B* from one and *a b* from the other) the hybrid $\left(\frac{A}{a}\,\frac{B}{b}\right)$ forms 4 types of reproductive cells (*AB*, *Ab*, *aB* and *ab*) which can enter into 16 combinations when the hybrids mate, as previously mentioned in connection with skin color. But when there are 3 genic differences, the hybrids $\left(\frac{A}{a}\,\frac{B}{b}\,\frac{C}{c}\right)$ form 8 different types of reproductive cells. These can enter into 64 possible combinations with each other in the formation of the offspring. Only one of these combinations produces the trait in one pure form or the other, as compared with 1 in 16 when there were only 2 genic differences.

Note again that the scarcity of the extreme types (that is, those with the pure traits) goes up out of all proportion to the number of genic differences. When there are 4 genic differences, the number becomes 1 in 256; with 5, it becomes 1 in 1024, etc. If then there were only 5 genic differences that separated most traits of the horse and the donkey, then only about 1 in a thousand offspring of the mule would be expected to show a trait of either parent species in pure form. All other offspring would show the trait in mixed form and would be more or less intermediate. Offspring that were strictly intermediate, or nearly so, would be most numerous, for the reason that the particular combinations that produce them would be most frequent, just as was true for skin color in man. This would apply to practically every trait, not just to one. Practically all of them would appear more or less intermediate in the offspring of the hybrid, just as they were in the hybrid itself.

It would therefore appear as though the hybrid had become constant and fixed. Results of this sort have in fact been got by breeders. For example, races of tobacco have been crossed, differing considerably in the size of their flowers, small in the one, large in the other. The hybrid offspring produced by the cross were intermediate in flower size, and their offspring in turn were all more or less intermediate. There was, however, an increase in the range of variation in the second generation, the very thing that would be expected if Mendelian segregation had been taking place in the hybrid of the first generation. The increase in range was not sufficient to include the more extreme classes, simply because the combinations necessary for their production

occurred less frequently than those by which the more intermediate types were produced.

The Mendelian principle applies to most hybrids regardless of how they are produced, especially those produced by the crossing of closely related varieties.[1] The individual genes distinctive of each parent segregate from each other in the hybrid and pass on to the next generation in pure form. The traits that then develop are determined by the particular type of gene or combination of genes that the offspring receive. This is true, also, regardless of whether the hybrids are some lower form of life, or whether they happen to be human beings.

But, it might be asked, how do ordinary people, those that are not "hybrids," transmit their inheritance to the offspring? And how are fundamental things like the backbone inherited? In answer to these questions, it should be pointed out first of all that, strictly speaking, the backbone is not inherited. The backbone is a trait, and like all other traits, it develops; it itself is not transmitted from parent to offspring. What is transmitted is the genes upon which the development of the backbone is dependent. The fertilized egg starts its development with many different kinds of backbone genes, possibly hundreds of them or even thousands. But practically all of those in one human being are of the same kind as in any other human being. Before a person reproduces, his reproductive cells receive a complete set of backbone genes (*A*, *B*, *C*, etc.), and when

[1] When very distantly related species are crossed the chromosomes often fail to segregate regularly, yet the genes within them doubtless remain uncontaminated.

two persons mate, each transmits to the child, or rather to the fertilized egg from which the child develops, a complete set of backbone genes which is practically the same throughout from each parent. The child therefore is pure in large measure for his backbone genes $\left(\frac{A}{A}\frac{B}{B}\frac{C}{C}\ldots\text{. etc.}\right)$; he receives a certain set of genes ($A\ B\ C\ldots$. etc.) from his mother, and a similar set ($A\ B\ C\ldots$. etc.) from his father. When the child in turn grows up, the backbone genes will pass to his reproductive cells, and this they will do according to the Mendelian principle. Allelomorphs will segregate from each other (A from A, B from B, etc.) and they will pass into separate reproductive cells. But a complete set of genes will pass into each reproductive cell, and every one will be of the same type (A, B, C, ... etc.). Any person with whom he mates will also have reproductive cells of this type, and the children of the next generation, the second under consideration, will be pure and of the same type $\left(\frac{A}{A}\frac{B}{B}\frac{C}{C}\ldots\text{. etc.}\right)$ just as were their parents. Accordingly, there are no distinct differences in the second generation, no Mendelian classes, to indicate that segregation has been taking place.

Direct evidence of segregation would only be manifest if the original parents happened to differ genetically. For only then would there be produced in the second generation the varied classes of offspring that are the visible evidence of Mendelian segregation. To be sure, all of the offspring would still have backbones, even though they had them different in length or in some other way; and it might still be asked whether

we had any evidence that the backbone itself, or rather the hereditary basis for the backbone, was inherited in Mendelian fashion. In order to produce direct evidence of the kind in question, one way of going about it theoretically, would be to cross an animal that had a backbone to one that had none; and furthermore to breed the hybrids and get offspring of the second generation from them. Only then would it be possible to get in the second generation some offspring that had backbones and others that had none, and so to demonstrate directly that *all* of the backbone genes segregated according to the Mendelian principle.

Not any backboneless animal would serve equally well for the cross. To bring out the facts clearly, it should be preferably one that had in place of the backbone some other structure, like the gelatinous rod from which the backbone evolved, a structure known as the notochord; and in place of the backbone genes (*A*, *B*, *C*, ... etc.), it should have others (notochord genes, *a*, *b*, *c*, ... etc.) to act as allelomorphs (partners) for the backbone genes in the hybrid $\left(\frac{A}{a}\frac{B}{b}\frac{C}{c}\ldots\text{etc.}\right)$. Needless to say, no such experiment could actually be performed. It would be impossible at the start to cross two animals so distantly related as one with a backbone and one without. Even if hybrid offspring could be got from the cross, it would be necessary in turn to mate them and to get large numbers of their offspring, enough to insure the production of the pure parental types. It would be necessary to raise countless millions of offspring in order to get the rare combinations that contained nothing but backbone genes, or

nothing but notochord genes. Only then would it be evident that all of the backbone genes had segregated from all of their allelomorphs in the hybrids, and that every one of them followed Mendel's principle.

These particular combinations would be rare because of the large number of genes that would have been shuffled in the hybrid $\left(\frac{A}{a}\frac{B}{b}\frac{C}{c}\ldots\text{etc.}\right)$. It would happen only in very rare instances that there would emerge from the shuffle the same two combinations that entered the hybrid, one combination consisting exclusively of backbone genes (*A*, *B*, *C*, etc.), the other exclusively of their allelomorphs (*a*, *b*, *c*, etc.). Even these combinations would not yet represent the offspring themselves, but only the reproductive cells of the hybrid. It would require the accidental union of two reproductive cells of pure type, rare in themselves, to produce an offspring of pure type, which would be exceedingly rare.

That there is a large number of genes involved in the development of the backbone is highly probable. A structure of such ancient standing as the backbone has had a long history. Its evolution took place over millions of years and must have involved the origin of many new genes, new in the sense that they arose by the change of pre-existing genes, a process known as mutation. In this way, the structure that was the precursor of the backbone gradually changed and became the backbone.

Mutation still affects the genes and causes changes in the backbone, changes in its length, width, details of shape, etc., and in this way gives us visible evidence of the genes themselves and of their variety. Every

other important trait has had a similar history. Every one is dependent in development upon a great many genes that came into existence by the process of mutation and that are still mutating occasionally. Strong evidence for this belief has been furnished by the observation of mutation in various animals and plants and in particular in a certain insect, Drosophila. This animal has been bred in the laboratory and kept under close observation for many generations; and through mutation a great many genes have become manifest in connection with its eyes, wings and other important organs. It is highly probable that in other animals also, every important organ is influenced by a large number of genes and is dependent in development upon them.

All this sounds very theoretical and of no practical value. Will it ever do the average man any good, or advance the welfare of the human race in any way? Possibly not in the immediate future. But the time must come when man will know himself and rise to higher levels, through knowledge of his own being. His hereditary make-up determines what he is by nature, both in his weakness and strength. He must know the hereditary basis for the good things as well as the bad before he can encourage the one and eliminate the other in the generations that are to come. At present, our knowledge of human heredity is pitifully limited. We know that it is dependent upon genes and that it all follows the Mendelian principle. This indeed is a very valuable bit of information and is indispensable to further progress in the field of heredity. But it is information of a general character that applies equally well to

all living things. It tells us nothing about the specific make-up of man or any other creature in particular.

Mendel could theoretically have told us how each gene for skin color was inherited, but he could not tell us how many of them there were. He could have told us that when the black and white races crossed, there would be no permanent mixture of the genes; but he could not have told us how many skin color genes there were characteristic of each race, nor how many classes of offspring mulattoes would produce. He would have been the last one to assert that mulattoes must produce 3 black to 1 white just because he found his pea hybrids gave a 3 : 1 ratio. Any such assertion would imply that the mulatto was hybrid for just one pair of allelomorphs $\left(\frac{A}{a}\right)$ and that each of the pure races had just one characteristic skin color gene (*A* and *a*).

Just how many such genes there are can only be determined after the races have crossed and produced offspring of the second generation, offspring that come from the mulattoes. They indicate by their ratio what sort of a hybrid the mulatto is, whether he is hybrid for one pair of allelomorphs, or for two, or for whatever the number happens to be. From this information it is possible to conclude how many characteristic skin color genes he received. If the ratio indicates that he is hybrid for two pairs of allelomorphs $\left(\frac{A}{a}\,\frac{B}{b}\right)$, then we conclude that he received two characteristic genes (*A B*) from one parent, and two (*a b*) from the other, and so there must be two skin color genes *characteristic* of

each race, that is, two in regard to which the races differ. Mind you, we do not know in advance how many genes there are and then figure out what ratio to expect in the second generation. The thing is just the other way around; we get the ratio in the second generation and figure out from this how many genic differences there are affecting skin color. So it is with all other cases of heredity. The results of a cross can only be told after we have got a certain amount of information pertaining to that particular cross. From this we can say something about the genic basis of the traits involved in the cross. In any event, we cannot by mere inspection of a trait tell what its hereditary basis is. Hybridization is necessary to this end. To say offhand that there must be just one gene for skin color, one for size, one for mental ability or any other trait, would be absolutely unwarranted.

In the study of human heredity, we are probably more interested in the basis for mental traits than for the mere physical. A certain man is intelligent. Will his children also be intelligent? This question overlooks the dual nature of heredity. The man's wife has to be taken into consideration. So must his wife's family as well as his own. If they both come from brilliant stock, exclusively so, their children might reasonably be expected to be true to type. It is when a man is one thing and his wife another that the problem of heredity comes up in its most acute form. What will the children be like, one or the other, or what possible mixture? It is not even the children of the first generation of such a cross that present the real problem; for it is entirely possible that they would resemble one

parent or the other, even though they were hybrids. It is the grandchildren, those of the second generation that present the real problem. They could not all possibly be of one type, supposing now for the sake of simplicity that their parents came from the same kind of a mating of unlikes. For the grandchildren would be the offspring of hybrids and hence would be varied in type. The number of different types, and the proportions of offspring belonging to each, would be determined by the extent to which their parents were hybrid; whether for just one pair of allelomorphs, for two, three, or for whatever number it happens to be. This in turn would be determined by the number of genes characteristic of the intelligent persons when compared with the ones who were not; for they are the persons who produced the hybrid offspring of the first generation. In brief, the offspring of the second generation vary just as for the negro-white or any other cross; and the extent to which they vary depends upon the genetic difference in the types that originally crossed.

But if the parents had originally been alike and of pure type, there could have been no genetic variation in the second generation or any other. If everybody were intelligent, intelligence would be taken for granted; and it would be a matter of surprise if anything but an intelligent child were born. Still, intelligence would be dependent upon genes, as is true of the backbone or any other trait, but everybody would have the same genes in common. It is only when some people have genes different from the rest that the problem of heredity presents itself. Then the real question is "Just how different are they

from the rest? Have they one kind of gene peculiar to themselves, two, three, or how many?" The answer to this question will tell us how complex is the heredity basis for the exceptional trait.

But people with the exceptional trait have by no means a monopoly on all the genes for intelligence. The average person has the intelligence that marks him as a human being and thus he has many, at least, of the numerous genes that arose by mutation during the millions of years consumed in the evolution of human intelligence. In an exceptional person, however, there are some genes that have mutated still further and so have become different from those of the average person. Not all of the "intelligence" genes have mutated still further, but only a relatively few. Neither have the old genes that they arose from disappeared as a class. They still exist in persons of average type, and in the hybrid they are allelomorphic to the new genes.

In studying the hereditary basis for exceptional ability, the problem is not to discover all of the genes concerned with the production of intelligence; this would be an impossible task. The problem is to discover just those that have mutated to the higher type. This can be done only through hybridization, by the crossing of the new type with the old. For then the offspring of the second generation show by their variety just how many genes there are distinctive of the new type, as compared with the old.

Controlled hybridization experiments in human beings are a practical impossibility, and so it will be difficult to work out the hereditary basis for exceptional mental

ability or any other trait. The family records that most people keep are of no particular value to the student of heredity. They give the names of their forebears and other scientifically worthless data. Only in unusual instances, as when an ancestor has had exceptional ability, or perhaps when he has had some very noticeable peculiarity, is any mention made of his traits. And then as a rule, nothing is given about other members of his parent's family or about his wife. What is wanted for scientific purposes is an accurate description of the traits in all ancestors for several generations back, as well as their schooling and other environmental factors that are known to influence the development of the trait.

It is possible, however, that we may be able to make some advances in the study of human heredity without the aid of complete family records, desirable as these may be. Take for example mathematical ability. Instructors of mathematics sometimes find that college students tend to fall into two rather sharp groups, a relatively few who are good at mathematical reasoning and a large majority who are not. In most other subjects, as history and biology, the intermediates are the most abundant. But in mathematics, the two extremes seem to be relatively more abundant. This conclusion is based upon more or less casual observation, but if it really holds it would indicate that mathematical ability had a rather simple heredity basis, in the sense that the exceptional persons have just one kind of gene which distinguishes them from the average type. For if there were several such genes, the intermediates would be relatively more abundant, as applies to the offspring of

mulattoes. It is being assumed that exceptional persons have in the past mated with those of average type, and that the population at present contains offspring of the second or later generations following upon the cross. Otherwise it would be impossible to say a thing about the hereditary basis of either type. Each would be distinct for the same reason that negroes and whites would be if they had never crossed. But the two types probably have hybridized in the past. If so the population now contains the various Mendelian classes that the hybrids are capable of producing, and if the intermediates are relatively scarce or lacking, then the hybrids are probably not of the more complicated type represented by the mulatto. Instead, they are probably of the simple kind with which Mendel dealt in his crosses, and the hereditary basis for mathematical ability is correspondingly simple. It is theoretically possible that people who are exceptional along mathematical lines have several genes, all of which are absolutely necessary for the development of their talent. In this case, there would be no intermediates. But when hybrids from a cross produce just the two types that entered the cross, it is much more usual for the two types in question to differ in a simple Mendelian manner, rather than in a more complicated way. It would therefore be fairly safe to conclude that mathematical ability was dependent upon just one special gene, rather than upon several, provided there were no intermediates and the requisite crossing had taken place.

A conclusion of this sort can be accepted only after careful study. It must take into consideration the action of environment. It is conceivable that most

people lack mathematical ability simply because their early training has been faulty. In this event, the exceptional person would be merely the product of training in the sense that anybody else would have developed the same ability had he received the same training. But if careful analysis shows that students who have had substantially the same history show a wide difference in ability, then there is probably a hereditary basis for mathematical ability. Undoubtedly the average man would be helped by good training and the naturally exceptional man hindered by poor training. In this event, the one would not appear very poor nor the other very good, but both would be more or less intermediate. If now, there were a distinct difference between students in the same classroom, who received about the same training, it would indicate (though not prove) that just one kind of gene distinguished the exceptional students from the rest. There would be some intermediates; but they would really belong to the one group or the other, genetically. Moreover, there would be few of them compared with the number in other subjects which required no special hereditary basis.

In the study of mental traits generally, whether it happens to be mathematical ability or any other special trait, the environment enters in as an important factor for consideration. For it is often difficult to tell how much an exceptional man owes to heredity, and how much to environment. Moreover, it is not sufficient for the student of heredity simply to find out whether the children of a brilliant man are also brilliant. Information of this sort could at best tell us whether or not there was any special hereditary basis for the tal-

ent under consideration. It would not tell us whether the trait had a simple or a complicated heredity basis, whether its development was conditioned by just one special kind of gene, or by more. This information can be arrived at only through the results of hybridization, the mating of the exceptional type with the average person. The hybrids so produced tell us nothing in themselves; but their offspring do, the offspring of the second generation after the cross. They must be carefully examined and classified, to see into how many different Mendelian classes they fall, and in what proportions they are produced: whether they fall into the simple ratios got by Mendel, or into the more numerous classes and more complicated ratios represented by the offspring of mulattoes. They must, furthermore, be reared in the same environment. Only then can we tell how many genes are distinctive of the exceptional type, and how complicated is its hereditary basis. This same procedure must be followed in getting at the hereditary basis for physical traits, as well as mental.

The Mendelian principle tells us nothing in particular about human inheritance; it is a general principle that applies to the gene, the unit of inheritance. The student of heredity cannot, by mere inspection of an animal or plant, tell us the hereditary basis of any particular trait. His position is exactly analogous to that of a person who is familiar with the principles of mechanics but who has not yet entered and studied in an engine room. The principles of mechanics underlie the operations of all machines, but the structure of these machines and their particular manner of operation are matters which demand separate study. Just so

in biology. Mendel's principle is at the bottom of all inheritance, but the precise details involved in any particular case have to be worked out. Sometimes the facts, after they have been got through hybridization, look very complicated, and do not at first sight seem to be amenable to the Mendelian principle. But in biology, as in the sciences generally, the same principle that applies to more simple events may also underlie the more complicated, even though this fact may not at first sight be apparent. It may require an extended analysis to show just how the simple principle does embrace all cases.

Mendel made a discovery which is just as fundamental in the world of living things as Newton's laws of mechanics in the lifeless. Whether or not an Einstein will appear in the field of biology to tell us that Mendel's principle, exact as it is, is only a close approximation to the truth, still remains to be seen. Certainly the more complicated cases of inheritance do not direct a damaging finger at Mendel. They point to something dependent upon his principle: multiple factors.

CHAPTER XII

THE ARTIFICIAL CHANGING OF A RACE BY "SELECTION," AND ITS LIMITS

Suppose a group of people should migrate to an island with the object in view of producing a very tall race of human beings by breeding methods, very much like those employed by practical breeders of animals and plants. To what extent could they succeed? Let us assume that the group who start upon the venture are themselves of average size; further that they and their offspring continue the experiment over a large number of generations, and that in each generation only such persons as are taller than the average of the previous generation are selected as the parents for the next generation, all others moving off the island. Would a race of tremendous giants ultimately come into existence?

It would, in fact, be found that the race did increase in size and that the increase was comparatively rapid during the first few generations of selection. But the rate of increase per generation would gradually die down and during the later generations there would be no further change. That is to say, selection would be effective during the earlier generations, but not during the later generations.

The results are somewhat comparable to what would

happen to the skin color of a mulatto population in which selection for lighter skin color took place. The mulattoes are hybrids and therefore produce a variety of offspring in regard to skin color. The lightest of these would, upon mating, produce offspring with a skin color lighter on the average than that of their mulatto parents and lighter than the average of the total offspring of the first generation (the offspring of the mulattoes). But further selection would produce little or no effect. In short, the skin color of the population would change on the average in the first generation of selection, but not in the second or later generations.

The genetic composition of the mulatto explains these results. The mulatto is a hybrid, having received white genes from his white parent, black genes from his black parent. He can be designated by the formula $\frac{a}{A}\frac{b}{B}$, where a b are the white genes and A B the allelomorphic black genes. By the process of Mendelian reassortment, mulattoes would produce children of various genetic classes, most of whom contained some black genes. But there would be some who contained only the white genes $\left(\frac{a}{a}\frac{b}{b}\right)$. They would be lighter than all the rest and lighter also than their parents. Their children would in turn be of the lighter type. If persons of their type exclusively reproduced the next generation, then the average skin color of the population would be changed. Selection would be effective.

But now the entire population would consist of persons who had nothing but white genes and further selection would be largely ineffective. Not that everybody

would be exactly of the same shade. Some still would be lighter than others, due to differences in the amount of sunlight to which they are exposed. But both the lighter and the darker persons now would have the same genetic make-up $\left(\frac{a}{a}\,\frac{b}{b}\right)$, and the one would not have lighter children on the average than the other. The differences in color would be due entirely to the environment (if we ignore the possible occurrence of an occasional mutation, and minor genetic differences, as between blonds and brunettes) and could not be inherited.

No new skin color genes could come into existence through the agency of selection. They are present at the start in the mulattoes. By Mendelian recombination, they become assorted into the various classes of offspring, some of which in consequence have more of them than others. Selection can isolate these classes; it cannot produce them. After the extreme type has been isolated, there can be no further effect of selection in changing the average amount of pigment in the population.

The effect of selection might extend over several generations instead of just one, but in this case it would take place through several small steps instead of just one large step. Thus the mulattoes with two white genes $\frac{a}{A}\,\frac{b}{B}$ might have children with three $\left(\frac{a}{a}\,\frac{b}{B}\text{ or }\frac{a}{A}\,\frac{b}{b}\right)$ and these in turn might have children with all four white genes $\left(\frac{a}{a}\,\frac{b}{b}\right)$. This increase is made possible through the process of Mendelian reassortment of genes. But by the same process the mulattoes with the two

white genes can produce directly some offspring with all four white genes; and so the full effect of selection can be arrived at either in one large step, or two smaller.

In a population consisting of a mixture of the two classes, it would be difficult to weed out through selection all but the one desired type, having all four white genes. Persons with three white genes would in some cases be confused with those who had all four white and it would be difficult to eliminate every last one from the population. But eventually they would all be weeded out and thereafter there would be no major effect of selection. The end result is the same as though the pure type with all four white genes had been selected in just one generation.

The results of selection for size would conform to a similar explanation. Size has a complicated hereditary basis. People of average size are hybrids and have a mixture of both tall and small size genes. Their offspring fall into various genetic types. Some have more genes for tallness than others, and by selection of the extreme type it is possible to change the average size of the population. After a race has been produced that has all the genes for tallness, then no further selection for size is effective.

It might be asked here, however, whether the extreme type does not itself undergo variation. Are not some children taller than others, even though they all come from the extreme type of parents having all genes for tallness? And do not these taller offspring in turn produce children who are also taller? The answer to the first question is very easy: yes, the children do differ amongst themselves, even though they do belong

to the same genetic class. No two individuals are ever exactly alike. This is a matter of common observation. But would selection of the taller types continue to be effective? The answer to this question involves a separate problem of its own.

It is true that selection of the taller offspring is effective so long as the parents are hybrid. But would it be if they were not hybrid? Bear in mind again the case of skin color, and remember especially that the extreme type isolated by selection is no longer hybrid. Could continued selection within this pure type change the race? Before a definite answer could be given to this question, very extensive and well controlled experiments had to be conducted. It was necessary to use lower forms of life for this purpose — man is very poor experimental material in genetics.

Especially favorable to the solution of this problem was plant material and in particular bean plants. For it was necessary to start the experiments with material that was definitely known not to be hybrid, and this was definitely known of bean plants. Hybrids are produced by the mixing of different races or strains through crossing; that is, through outbreeding. Bean plants very seldom outbreed. Instead, a single plant is both "mother" and "father" of all the seeds produced by that plant. The pollen is not carried from one bean plant to another by insects or wind, but it remains on the plant that produced it and serves as the male element for that plant. The seeds are therefore produced by self-fertilization, the closest form of inbreeding possible. So long as self-fertilization continues generation after generation, the offspring of a given plant

cannot receive from some outside strain genes different from the one to which they belong and so cannot become hybrids. But even if crossing did take place, as occasionally happens in beans, the strain would remain hybrid for only a relatively short time upon the resumption of self-fertilization. For all of the offspring produced by the hybrids would not be hybrid. Only some would be. Others, through Mendelian reassortment, would be pures; and it can be demonstrated mathematically that in a relatively small number of generations all of the hybrids would automatically be eliminated from the strain through the process of self-fertilization. A given bean plant, therefore, is in all probability pure throughout its entire germ plasm, both because crossing is very rare, and because self-fertilization rapidly eliminates all hybrids from the race.

The offspring of a given bean plant, however, are not all exactly alike in their outward appearance. Take, for example, the size of the beans. It is a matter of common observation that no two beans in the same pod are of the same size, those at the ends being smaller than those at the middle. In addition, some come from the larger of the pods and are correspondingly large. If you went to the trouble to measure all the seeds of one plant for length, you would find a regular gradation from the smallest to the largest extreme. You would further find that those of average size were the most numerous as a class, and that those that were smaller or larger than the average became less and less numerous in accordance with the extent to which they departed from the average.

The problem before us now is this. Suppose you

picked out the largest bean on the plant and grew it, would it produce seeds of larger size on the average than those of the plant from which it came? This experiment in fact has been performed,[1] and it was found that the offspring produced by the largest seeds were no larger on the average than those produced by other seeds of the same plant. The person who performed the experiment went further. For it occurred to him that possibly there might have been a slight increase in average size, but that it was so small that he could not measure it. In order to test this possibility, he selected the largest seeds for several generations in succession, with the object in view of accumulating and making more pronounced any slight increase that might occur in a single generation. He found, however, that the average size of the race was no greater at the end of selection than at the start.

If you yourself wanted to repeat the experiment just described, you might begin by going to your grocer's for a quart of beans, and after picking out the largest one, plant it, wait for it to grow and then gather the seeds that it produced. If now, you measured these seeds, you would probably find that their average size was greater than that of the quart with which you began and you might think at first that your result was not in agreement with the one above described. But if you had the patience to carry your experiment through another generation, and again planted the largest seed you could find, you would discover that it produced seeds no larger on the average than did the parent plant.

[1] By W. Johannsen, of The University of Copenhagen.

You might have begun your experiment by picking out the smallest seed from the original quart and a medium sized one, in addition to the largest, and you probably would have found that they produced respectively seeds that were on the average small, medium, and large. The seeds of each of your three plants would produce seeds in the next generation which had the same average size as those of the plant from which they came, regardless of what sizes you now selected for planting. Moreover, you could now grow any number of plants from each of the three that you began with, and grow them for any number of generations, and you would find that the average seed size of any plant was the same as that of the plant from which it was originally derived, small, medium, or large, as the case might be. You would, in other words, now have three races or rather "lines" each of characteristic average size. If you picked out and grew any one of the thousands or possibly millions that belonged to the same line, you would find that it produced seeds of the same average size as did any other of its line, namely, the size characteristic of that line.

When you started your experiment you would not have known much about the origin of the quart of beans that you bought. They would probably have come from a large farm with many bean plants, the seeds of which were not carefully kept separate by the farmer, but were gathered and mixed up with each other. The quart of beans therefore would have contained seeds from different plants all of which did not necessarily belong to the same line. The chances are that they belonged to a number of different lines, including the three that

you now have in your possession. These you isolated from the mixture and from each other by the simple act of selecting from the quart just one seed belonging to each line, and then keeping their progeny separate.

It is apparent now why you got an effect of selection at first, when you grew the largest seed in the quart. By isolating the largest line from the rest, you got progeny of greater average size than that of the mixture, the average size of the mixture being that of all the lines, smaller ones included. It is also apparent why you got no further effect after the first generation. One selection was sufficient for isolating the largest line from the rest. To be sure you knew very little about the mixture of seeds with which you began, in point of their precise origin. But there is one thing you could have been sure of; namely, that any seed which you isolated was derived from a plant which produced this seed by self-fertilization; and that the ancestors of the plant had been self-fertilizing for many generations, since such is the habit of bean plants. The particular plant that you isolated could therefore not have been a hybrid; it must have been of pure type. Moreover, the plant continued to reproduce by self-fertilization after you isolated it and the progeny must all have been pure, regardless of how many generations there were and how many plants there were in each generation. What is more, they were all of the same genetic type, because the entire line was derived ultimately from the same seed. The line that you isolated and grew is technically known as a "pure line."

In brief you began with a mixture of pure lines and you got an effect of selection in the first generation.

But thereafter you got no further effect. By your first selection you isolated a pure line; but by further selection within the pure line, you produced no further effect.

There was no way of telling from mere inspection that the original quart of beans was a mixture of different pure lines, each having its own average size. If, indeed, there had been just two lines in the mixture, one very large and the other very small, it would have been perfectly apparent that you had two distinct kinds of beans. But, there are intermediate sizes connecting the two extremes, and you get the impression that you have just one kind of bean which varies in size.

Not only are there pure lines of intermediate size connecting the two extremes, but in addition the beans within each pure line vary in size, and the larger of one pure line is just as large as the smaller of the pure line that is next in point of average size. That is to say, if you measured the beans of any two consecutive pure lines, you would find that each was of a certain average size, but that there was no strict conformity to this size, some being smaller than the average, others larger. These deviations from the average tend to make the bean sizes of one pure line pass by imperceptible gradations into the next. In fact, the largest beans of one line exceed in size the smaller of the next higher class and there is in consequence an overlapping of sizes which makes it impossible to decide by mere inspection whether a particular bean within the range of the overlap belongs to one pure line or the other. To decide this point you would actually have to plant the bean and find out the average size of its offspring. These

would conform not to the particular size of the parent seed but to the average of the pure line to which they belonged. The parent seed departed from the average of its class not because it was different in its hereditary make-up from the others of its class, but on account of the influence imparted by the particular environmental conditions under which it was grown, an influence which cannot be transmitted to its offspring.

In the mixture of pure lines there is an imperceptible gradation in the size of the beans from the very smallest to the largest just as there is within a pure line itself and it might appear upon superficial inspection as though the variations were of the same nature in the two cases (in the mixture of pure lines, and in the pure line itself). But in the pure line, the variation is strictly environmental. In the mixture of pure lines, on the other hand, the variation is due to two causes: first, actual genetic differences between the pure lines and second, environmental variations within each line. So long as selection has genetic differences on which to operate, it can be effective. But once it is limited to purely environmental differences, it is absolutely without effect.

Very extensive and well controlled experiments have actually been performed on beans establishing the above mentioned point.[1] But it might be objected that beans are one thing, humans quite another, and that the things that apply to the one do not necessarily apply to the other. True enough. But they have this in common: the stuff which constitutes their inheritance is made up ultimately of separable particles, the

[1] By Johannsen.

genes. The pure line experiments on beans have established a very important point in regard to the ultimate units of heredity namely, that they are extremely stable bodies not subject to continuous variation from one generation to the next. If now, this conclusion applies to beans, it in all likelihood applies equally well to man.[1] For it is to be remembered that the genes in both cases are contained within the chromosomes and are subject to the same principles of inheritance. In fact, it was in plants of the bean family that Mendel first established his principles of inheritance. It is true that his experiments were not conducted with the object in view of testing the stability of the gene. But his experiments did start a vast number of other experiments and observations on many forms of life, man included, and from this vast body of evidence it became apparent that the ultimate units of inheritance were contained in the chromosomes and that they were subject in their mode of inheritance to the principle that Mendel had discovered. It would now be rather odd if the genes of man and other forms of life were alike in one fundamental respect, their mode of transmission to the offspring, but not in another, their stability; especially in view of the fact that other experiments have been conducted with the object of testing the stability of the gene and whenever they were properly controlled, they confirmed for other forms of life the results found to apply to beans.

Man, to be sure, has many peculiarities as a species.

[1] Recent work has indicated that genes of some organisms mutate oftener than those of others, but even in the most mutable the great majority of the individual genes are exceedingly stable.

So have other species. But all forms of life, no matter how simple or complex, or how diversified, have certain things in common, the fundamental characteristics of their organization. All are members of one great family distinct from the lifeless world. The biologist sees evidence of this similarity in their microscopic structure — the cells of which they are made and the chromosomes within the cells. And when he discovers a principle that applies to one he often finds that it applies to all others that are put to the test. When now he finds genes to be stable in beans, then he also expects them to be stable in man.

It is true that there are no pure lines in man in the sense that there are in the bean family. Man outbreeds too much for that. But the outbreeding process, so far as we are aware, in no way influences the fundamental properties of the gene. It merely results in a different distribution of the genes in the individual and makes him hybrid. Because of this, a great many of his traits are subject to variation, and not because of any variation in the genes themselves. Whenever he is pure for the genes that affect a particular trait, then the trait is no longer subject to heritable variations; for there are no longer the diverse genetic classes of offspring that result from hybridity of the parents. It is for this reason that the race could not be made indefinitely tall under the influence of selection.

It will be seen now, that it is one thing to get an effect of selection in a hybrid race; quite another to get it in a pure race. In the one case, the offspring fall into various genetic classes on account of the hybridity of their parents and they vary accordingly. In the other

case, the variation cannot be traced to any such cause. For the parents are pure, not hybrid; and the offspring all belong to one genetic class. They start out life with exactly the same hereditary equipment. Any differences which develop between them must be due to differences in their environment. But increased size or any other variation thus brought about cannot be transmitted to the offspring. The environmental variation, in other words, cannot be inherited. The experiments on beans leave no doubt as to this. Besides, these experiments give the very results that are expected on theoretical grounds. For the environmental variation is an acquired trait, like tanned skin; and should it be transmitted to the offspring, it would mean that there was an inheritance of acquired characteristics. This the modern student of heredity has come to reject on various grounds. The selection experiments on beans merely furnish further grounds for his belief. The negative results of these experiments are, in fact, as strong evidence as any there is against the inheritance of acquired characteristics, and must always be born in mind in this connection.

Despite the limitations that there are on selection in changing a race, practical breeders have accomplished truly amazing feats through its agency. Cows that produce over half a ton of butter fat a year, hens that lay an egg a day, sweet peas and roses of exceeding beauty and bewildering variety, these and many other results have they got through the magic of selection. Breeders seem, moreover, to be able to get almost anything they want; tremendous dogs for hunting big game or little ones for ladies to hold in their laps; horses that

do a half mile in less than a minute or that move a heavy load almost through sheer bulk. They seem to hold the race in their hands and to get a product very different from the thing with which they begin. To be sure, they are very patient. Their work extends over many years and one may only begin a thing that many others help to carry to completion in later generations.

The history of the practical breeder's work is often veiled in a cloak of obscurity. Some things came from China many hundreds of years ago — tea, the silk worm and the primrose, among others. Corn has been under cultivation ever since the dawn of history and was in a high state of development at the hands of the American Indians before ever the white man arrived. The hen, some think, came originally from India, but whether from one original wild race, or through the crossing of two is not definitely known. The cat was known to the ancient Egyptians. Primitive man already had the dog as a companion. Possibly he domesticated the wolf by simply capturing him when he was a cub and so produced the ancestor of the dog. But again, whether there was just one such hypothetical ancestor, or whether different varieties of wolves were crossed, is not definitely known.

Even after the various domesticated races of animals and plants came into the possession of the Western European, there was often no definite record made of exactly what they were like in a good many instances, nor of the further changes that they underwent. The breeder of domesticated animals was and still is a practical man, not a theoretical scientist. He is more interested in getting his results than in how he gets

them. In consequence, he has often left us no records of real scientific value. Sometimes he crossed different races and produced hybrids from which he got by selection other types made possible by Mendelian recombination. When the species was already more or less hybrid as it often was, he found that selection by itself sufficed. Or, still more simply, he merely looked about and found already existing in nature something suited to human needs and requiring no further changes other than those that might come from favorable cultural conditions.

In very rare instances, something genuinely new suddenly arose not attributable to hybridization. A case in question is the very short legs of a certain breed of sheep, so short that they save farmers the trouble of building high fences around enclosures from which ordinary sheep could escape by jumping. The new breed of sheep apparently came from the clear blue sky without previous trace in the particular stock of sheep in which it arose. It appeared unexpectedly and independently of any attempts at producing it through selection; it was merely seized upon and saved after it made its appearance. Changes of this sort, known as mutations, probably have arisen from time to time in domesticated races of animals and plants and have been of value to the breeder. This was especially true in the case of races that were kept under observation for many centuries, during which period the mutation process was given sufficient time to produce many valuable changes. Some of these were doubtless by large, others by a series of small steps. Not in all instances have they been valuable. Sometimes they de-

formed the plant or animal in which they appeared and caused it to be cast aside as a freak or monstrosity.

Whatever the methods of the practical breeder may have been, one thing is fairly certain, he did not and could not produce by mere selection anything that was not already in existence. Sometimes the thing he got was in full bloom and readily apparent from its outward appearance. But often it was in the more hidden form of scattered possibilities in the race, possibilities in the sense that they were the hereditary units, the genes.

When the breeder produced a tall race from one of average size he did not create the genes for tallness. He merely accumulated them through the process of selection. Once he produced the extreme type made possible by the genes already in existence, he could go no further. The only possibility that then remained for further progress was the origin of new genes, again not through selection, but through a totally different process — mutation. This was a process which the breeders could not control in any way, for it was slow and sporadic in character and indeed even unknown to many of them. The stock with which the breeder begins is often hybrid, either purposely made hybrid by him, or already so as it comes to his hands. The extreme types are nothing but the Mendelian classes which the hybrids are capable of producing through recombination of genes — assuming now that mutations have not occurred.

There are certain things though which the breeder is able to do and which probably would make him hesitant in accepting any such limitations. He might argue that if selection from hybrid stock is capable simply of

isolating Mendelian classes — for such in substance is the contention — then his job ought to be finished in one generation. For in one generation the hybrids can produce all possible Mendelian classes. Still, he will tell you, he can carry the process of selection beyond the first generation and he can get many things that did not appear early in the game by just hammering at it long enough. This is true. What is more, the process of selection seems to predispose the race towards changing further in the direction that selection got it started on. Thus, once he has got it on the way towards tallness, it seems to continue going, much like a ball that continues to roll from the impulse originally imparted to it.

An illustration will suffice, possibly, to make clear why this should appear to be so, as well as why selection can be carried effectively over several generations, beginning with hybrid stock. Take again for the sake of simplicity the mulatto and selection for lighter skin color from original mulatto stock. Mulatto parents, each having two white genes, can produce offspring of the extreme type having all four white genes, as well as of the other extreme having no white genes at all (but four black in place of them). These extremes are rarer than the intermediates having one, two, and three white genes and if the number of offspring were limited, only the intermediates would make their appearance. This point has already been mentioned, as well as the further point that from the offspring having 3 white genes, others having all four could be produced in the next generation, and that the effect of selection could therefore be carried over two generations. But note a further fact. Offspring with three white genes are more likely

to produce others with four than were the original hybrid parents (who had two), simply because it is a smaller step from 3 to 4 than from 2 to 4. They are, for the same reason, less likely than the mulattoes to produce offspring having only 2 white genes or less. The offspring tend to vary about the average of their immediate parents in the number of genes they receive and so each generation would naturally enough vary in the direction of selection, until the extreme Mendelian class was secured.

But the class in question would actually be got with fewer total number of offspring if selection is allowed to take place over several generations, than if it is forced to get the desired class in just one generation. For, in order to insure the production of an extreme class in one generation by Mendelian recombination, it would be necessary to raise enough offspring to get not only this class, but every other class as well. For with limited numbers, there is no particular reason why just the one extreme should make its appearance rather than the other along with all the intermediate classes. On the other hand, if selection takes place in several steps, the one extreme makes its appearance without the other and the relatively large number of offspring are avoided that would be necessary to insure the production of both extremes and all the intermediates. It is possibly on this account that selection seems to predispose the race towards changing in the desired direction and to cause something to come into existence that would not otherwise have appeared. Furthermore, as the number of genes goes up that characterize the extreme classes, the number of offspring necessary to insure their ap-

pearance in a single generation goes up out of all proportion, and it becomes practically impossible in an ordinary experiment to get the required numbers of offspring when the number of genes involved gets beyond a dozen or so. This difficulty does not hold, to such an extent at least, when the selection experiment is carried over several generations.

It seems reasonable to conclude then that selection does not actually predispose a race to change in a certain direction, but only apparently so. There is still another thing about selection that appears rather surprising. It is possible through it to change a race first in one direction, then back again in the direction from which it came, and to do this back and forth at will. Now if it is true that the extreme type got by selection is merely an isolated Mendelian class, then this sort of thing would not be expected, especially if the class in question were uniform in its genetic constitution and of pure type. Further selection, no matter in what direction, whether back again or further along, should be ineffective, for the same reason that it is ineffective in a pure line. And in fact it would be, if the experimenter could be sure that he had actually isolated the extreme type, and this type only. But in point of fact, it is difficult to be sure of this. If some hybridity still exists, or if some individuals in the race are not actually of the extreme genetic type, but only apparently so, then it is possible by selection to return the race to the original type. For if either of these things is true, it means that there are still in existence some genes of the old type, scattered about in the population; and it is possible by selection to concentrate these in the course

of several generations into a few individuals and to get from them again a race of the original type.

When hybridization is combined with selection, it is possible to get from two races extreme types which neither race by itself was capable of producing. Thus, hybrids have been produced by crossing two races of tobacco differing in the size of their flowers. From the hybrids, offspring were got some of which were of larger flower size than that of the large race, and others of smaller flower size than that of the small race, as well as intermediate types. This result is not so surprising when it is remembered that each race contained genes for size that the other lacked, and by crossing and Mendelian recombination it was possible to get all the large size genes together into some of the offspring and all of their allelomorphic small size genes into others, and so to produce the two extreme types, each more extreme in its direction than the original parent races.

This sort of result cannot always be got. Take, for example, the negro-white cross. The mulattoes from the cross produce a varied type of offspring, but none more extreme in darkness than the negro or than the white race in lightness. The reason is that the negro race has all the genes for darkness and the white race all the genes for lightness. The best that the mulattoes can do in the way of producing extreme types through Mendelian recombination is to give some of their offspring nothing but dark genes, others nothing but light genes, as was originally their distribution in the dark and light races respectively.

Take, on the other hand, a case like this. Suppose two races of man had become isolated on separate

islands and were of intermediate skin color. It would be entirely possible for each race to be of pure type, from the genetical viewpoint, in spite of their outward resemblance to the mulatto, a hybrid type. For neither race need have all the genes of one kind or the other, but one race might have one combination, the other another combination, in each case, however, a combination of pure type. To use symbols, one would be $\frac{A}{A}\frac{b}{b}$, the other $\frac{a}{a}\frac{B}{B}$, where the large letters designate genes for dark skin color, the small letters genes for light skin color. Note that neither race has all the negro genes nor all the white genes; and further, that each is of pure type in that its allelomorphic genes are of the same kind (that is, those represented above and below a given line in either formula). So long as the two races remained separate, it would not be possible by selection ever to derive from either of them a type that was anything but intermediate (mutation excluded), because they are of pure type, and not hybrid like the mulatto. But now let the two races cross. Hybrids are thereby produced $\left(\frac{A}{a}\frac{b}{B}\right)$ essentially similar in their genetical make-up to mulattoes, and from them it is possible to obtain offspring of the extreme types, some having nothing but the dark genes $\left(\frac{A}{A}\frac{B}{B}\right)$, others nothing but the light genes $\left(\frac{a}{a}\frac{b}{b}\right)$. The case is essentially similar to the one previously mentioned in connection with the tobacco plants, in that neither of the two original races

has a monopoly on all of the genes characteristic of the extreme possible types. It is possible to pool the genes through hybridization and then to segregate the genes of the extreme types through the hybrids. Where the extreme types already exist before hybridization as in the negro-white cross, it is not possible through hybridization and selection to go any further in the direction of the extremes.

It will be apparent now that selection has its limitations. It cannot call new genes into existence; it can only operate on those that are already at hand. A negative conclusion, you say, only of a destructive kind, and rather discouraging for those who rely upon it to improve races for mankind, and maybe mankind himself. But so it is with science, sometimes. The conviction had to come that magic could not cure disease before science could undertake to cure it. Yet the case against selection is not quite so bad. The modern geneticist has not shown that selection is worthless in the improvement of a race, he has merely shown that it has its limitations. It is well that he should tell us what selection cannot do, as well as what it can. For then we are spared the trouble of trying to make it do the impossible, and we use it for what it is worth. It still has tremendous possibilities. In almost every race, there exist the scattered possibilities for its improvement; and by means of selection, or hybridization and selection, the breeder can bring them together into all conceivable forms and combinations, suitable to the needs and fancy of man. Of this fact, the workers at a certain experimental station in Sweden have in recent times given a convincing demonstration. By a careful

study of wheat, they were able to discover varieties already in existence that were suitable to the many different soils and climatic conditions of Sweden, or that furnished the material for crosses suitable to these ends.

In the case of the human race, the possibilities for improvement are still more far-reaching, especially in the field of mentality. Here we find the possibilities of a Shakespeare, a Pasteur, or an Einstein. Only after selection has produced these, and possibly even greater, will it have reached its goal. Then it will be time enough to wait for the slow process of mutation to carry the race further. Who knows but that the process of mutation itself might not by then be well under control?

INDEX